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The new Helio Ocean


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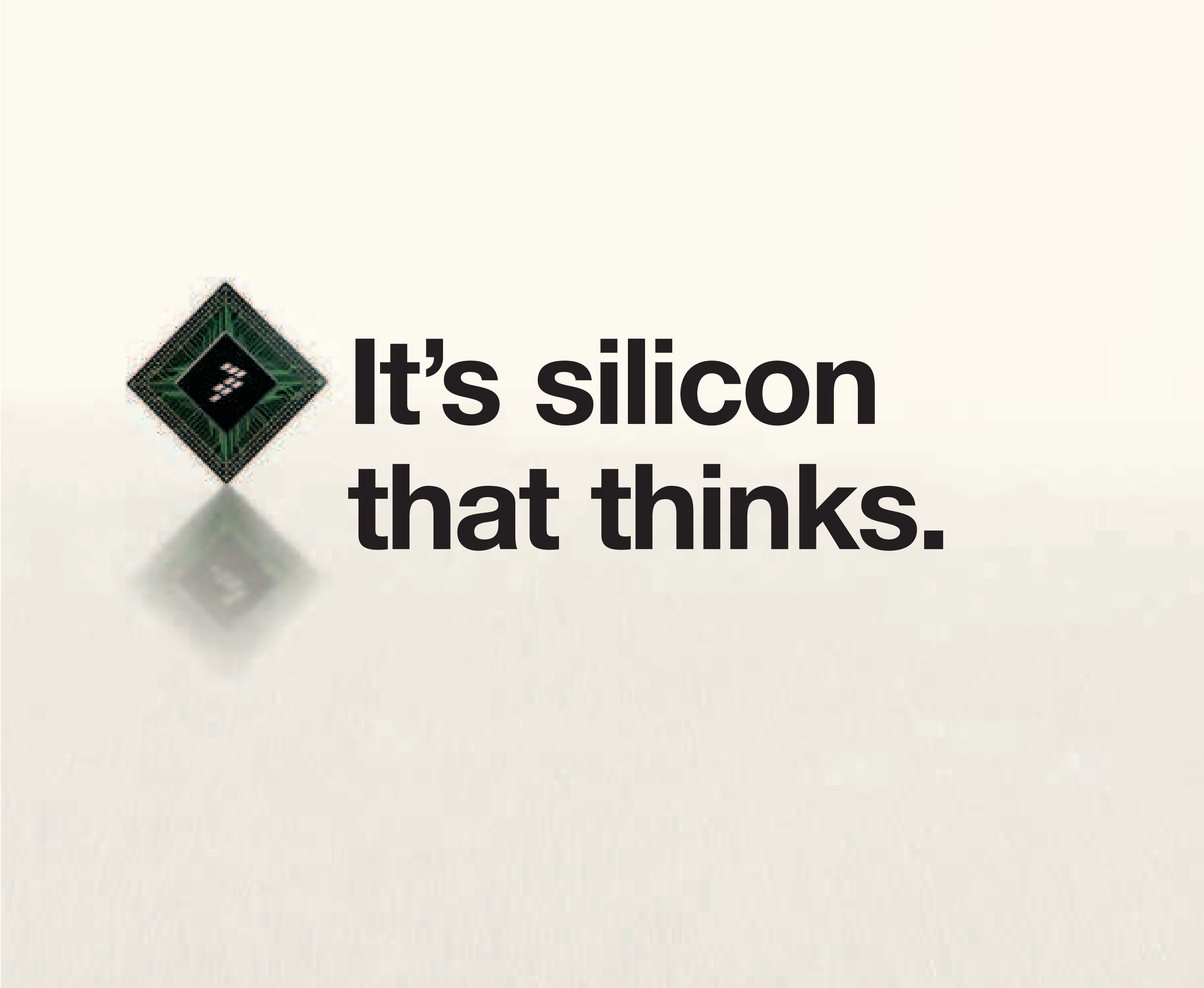
Cover photo by Toby Pederson



It's a digital home that automatically monitors security, adjusts temperature and adapts lighting. It's a car that responds to the driving situation hundreds of times faster than its human driver. It's a wireless network that speeds video from laptops to mobile phones. It's innovations, like MRAM, a radically new way of managing memory that completely redefines what an inanimate object can know and do. It's silicon in the hands of engineers at Freescale. 25,000 people dedicated to making the world a smarter, better connected place. Now that's thinking. freescale.com

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Technology Review, Inc., the authority on the future of technology, identifies emerging technologies and analyzes their impact for technology leaders. Technology Review publishes *Technology Review* magazine (the oldest technology magazine in the world, founded in 1899) and the daily website technologyreview.com; it also produces live events such as the Emerging Technologies Conference. Technology Review is an independent media company owned by the Massachusetts Institute of Technology. The views expressed in our various publications and at our events are often not shared by MIT.

De Technologia non multum scimus. Scimus autem, quid nobis placeat.

Contributors

Roger Scruton is a leading conservative British philosopher who agreed to explore, in this issue's essay, basic questions of ethics as they pertain to technology, and in particular to the life sciences *("The Trouble with Knowledge," p. 78)*. "Science explains the world; technology changes it; and philosophy questions the change," he says. "Technology may solve one problem by causing another, and until we have a conception of the 'fixed points' in our world, we can have no real understanding of which changes to avoid. But one of those fixed points is human freedom, which by its very nature refuses to be fixed. This is a paradox that infects, whether knowingly or not, many of the debates over new biotechnology. In exploring these debates, I find myself torn in many directions but find a comfort in human finitude of which not every advocate of biotechnological research will approve."

Scruton entered the University of Cambridge to study natural sciences in 1962 and has since followed a varied career as an academic philosopher, writer, journalist, and businessman. He is currently a research professor at the Institute for the Psychological Sciences in Arlington, VA, and has written widely on aesthetics, politics, and the philosophy of mind.

Roger Black is a living legend in the magazine world and a good friend of *Technology Review*; two years ago, he led the redesign of these pages. As we planned this issue on design, we began wondering what Roger thought about the current state of graphic design on the Web. He obliges our curiosity with a short essay *("Help Me Redesign the Web," p. 60)*. "Considering that the Internet is more like the phone than a newspaper," he says, "it seems odd to me that some folks are so possessive of it. The fact is we can all use it, and as the quality of software and connections improves, we can do just about anything we want with it. You can sing opera into it, or solve obscure riddles of quantum physics, or watch a movie. These things don't cancel each other out, any more than

they do in the analog world. All ideologies are at large on the Internet, so I have become an agnostic."

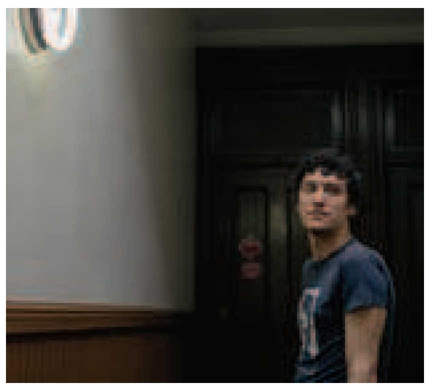
Roger is known for his work at *Rolling Stone* in the 1970s, *Newsweek* in the 1980s, and MSNBC.com in the 1990s. He has designed or redesigned more major American magazines than any other designer.

It came as little surprise to **Daniel Turner** that Apple proved reluctant to coöperate with this magazine as it pursued a story about how the company does what it does so well: design *("Different," p. 54)*. "Apple has rarely even admitted the existence of upcoming products, let alone discussed the design process," says Turner. "In the course of my research, I found that this was due only in part to trying to maintain an advantage over competitors; source after source stressed other factors, such as the publicity-

shy nature of Jonathan Ive, Apple's design head, as well as company CEO Steve Jobs's desire to maintain the image that design icons such as the iPod were group projects." Turner has covered Apple (and sometimes even sniffed out some secrets) for *eWeek*, *Salon*, *I.D.*, and others; his work has also appeared in the *New York Times*, *Feed*, *Nerve*, the *Boston Book Review*, *Lingua Franca*, and *Mountain Biking*.

Sam Weber did the illustration *(p. 79)* that accompanies Roger Scruton's essay on ethics and technology.

"I always love illustrating science topics," says Weber. "My father is a scientist, and I remember getting really excited about science at a very early age. For me, science and technology get especially interesting when they are framed within the context of ethics and morality."



Born in Alaska, Weber grew up in Canada and currently lives in Brooklyn, NY. His clients include the *New York Times*, the *New Yorker*, *Wired*, Herman Miller, and Sony/BMG.

What's New on Our Website

Audio Versions of All Stories

In mid-April, we added a new capability to the site: text-to-speech. With this technology, visitors are able to hear an audio version of any story on our site, read by a computer-generated voice. Each audio file can be streamed directly from the site and listened to over the Web; alternatively, it can be downloaded as a podcast to an iPod or other music player.

The technology that produces the readings was developed by AudioDizer, a Seattle-based company with an MIT connection: one of its founders, Harpreet Marwaha, is a student at the Sloan School.

We are, we believe, the first media company to offer this combination of text-to-speech and podcasting. To use the feature, just go to any story and click the Audio tab.

Accolades for the Site

In March, TechnologyReview.com was recognized in two categories at the inaugural Magazine Publishers of America Digital Awards.

We were named first runner-up in Best Online Video or Video Series for a series of videos, produced by Upland Productions, on a range of emerging technologies.

We were also named second runner-up for Website of the Year in the Business/News category. What pleases us most about this recognition is the great quality of the company we keep: the award was won by Time.com, and the first runner-up was BusinessWeek.com. Our fellow second runner-up is Forbes.com. These are sites we greatly admire; our Web team is honored to have been mentioned along with them.

Video: Tim Berners-Lee

In the March/April 2007 issue of *TR*, writer John Borland explored new technologies meant to make online search more intelligent (*"A Smarter Web"*). Part of that trend is a project called the Semantic Web, which has no greater champion than Tim Berners-Lee, the inventor of the Web itself. In an eight-minute video, he tells us why he thinks a sea change based on new ways of accessing and manipulating data is upon us—and why it could be even bigger than the change brought about by the first incarnation of the Web.

A Note from Richard Stallman

Larry Constantine's "Notebook" essay on open-source software ("The Open-Source Solution," January/February 2007) inaccurately describes me as an "open-source pioneer." No way! I'm not even a supporter of that.

In 1984, I founded the Free Software Movement, which aims to give computer users the freedom to share and change the software they use. In 23 years, we have made substantial progress toward that goal: our GNU operating system, combined with the kernel Linux, makes it possible for you to use a computer without letting proprietary software developers have power over you.

Open source refers to a completely different idea, which does not aim for freedom or social solidarity but merely wants to make software more powerful and reliable. Those practical goals are useful, but we must not subordinate ethical issues to engineering.

Contrasting free software (or open source) with "commercial" software is a second misunderstanding, like contrasting tall people with redheads. Commercial software means software developed by a business. Many important free (and open-source) programs, including OpenOffice and MySQL, are commercial.

Richard Stallman
Cambridge, MA

How to contact us

E-mail letters@technologyreview.com
Write *Technology Review*, One Main Street, 7th Floor, Cambridge MA 02142
Fax 617-475-8043
Please include your address, telephone number, and e-mail address. Letters may be edited for both clarity and length.

Fiction

As a fan of your publication, I read with interest your foray into publishing science fiction ("Osama Phone Home," by David Marusek, March/April 2007). Although the concept seemed interesting, as a fan of the genre, I have to say there are better short stories out there. I just don't see the upper middle class ever mobilizing in the way Marusek describes: they are, in general, too afraid of losing their hard-fought niche to risk their families' comfort for the abstract notion of patriotism. Much more interesting—and plausible—would be the same story centered on a group with a different shared interest—people with access to funds, motivation to remain loyal to one another, and so on. I did appreciate the creative daring of both the author and the characters, though; I think there's value to those sorts of everything-on-the-table discussions about how we might use technology to solve problems in interesting ways. I just hope that those discussions don't lead to solutions that so clearly threaten our civil liberties. I look forward to reading more fiction in your pages, and to enjoying more of this kind of exploration.

Sam Nekrosius
Chicago, IL

I enjoyed Marusek's short story, with one exception: he violated the principles of quantum mechanics when he asserted that "researchers found that if they made the zinc oxide molecules really tiny, they could produce a much more pleasant sunscreen." To shrink the molecule, you would need a different number of electrons and protons. But then it wouldn't be ZnO. Substitute the word "particles" for "molecules," and the statement is correct. Zinc oxide particles around 200 nanometers (a lot larger than a single molecule) are a great compromise between absorbing UV, scattering light, and being transparent when properly suspended in oil-water emulsions. Zinc oxide particles in the one-micrometer range result in the opaque sunscreen of yesteryear. It was easy for me to spot this error, since I use a variety of analytical techniques to study colloids and nanoparticles. Still, the story was fun to read.

Bruce Weiner
Holtsville, NY

Predicting the Internet

In his recent editor's letter "On Science Fiction" (March/April 2007), Jason Pontin writes that "Older computer scientists and electrical engineers such as Marvin Minsky and Seymour Cray, born in the mid-1920s, pursued a vision of humanlike artificial intelligence and mainframe computing popularized by science fiction after World War II (see Isaac Asimov's 'Multivac' stories)." Minsky and Cray just missed the right story, as did a lot of other folks. Murray Leinster, in his story "A Logic Named Joe," predicts a version of the Internet and the home computer. Astoundingly, it was published in 1945.

Alan Dean Foster
Prescott, AZ

Taking Exception to the Rules

I enjoyed Jason Pontin's editor's letter about the expression of ideas ("On Rules," January/February 2007). But in closing, he writes, "The best expression of ideas occurs in forms that are strict and simple." I take issue with this notion and the thrust behind it: the belief that ideas should be conventionalized and rule based. Envisioning ideas in a form—as expressed by a software language or by a poem—limits the possibility of expression and the development of new form.

In my opinion, it only makes sense to think of "mature" ideas in a strict and simple form. Ideas that are under development are messy and complicated things. It is the process of interacting with, and distilling, an idea that shapes it into a useful form.

Michael H. Felberbaum
Milford, CT

Correction

An item in the "10 Emerging Technologies, 2007" feature in the March/April issue incorrectly identified Ed Boyden as a postdoc at Stanford University. He was a Stanford graduate student when he performed the research described.

From the Editor

On Beautiful Machines

Well-designed technologies are minimally complicated

MARK OSTOW

I am writing this column on my new 17-inch Apple MacBook Pro—and oh, man, it's a beautiful machine.

I have owned this model of computer before. I used my old MacBook Pro until the other day; but sadly, foreign travel dented its aluminum casing, dulled all its surfaces with dust and oil, and reduced its screen to flickering fog—and as it ceased to be new, I became insensible to its virtues. But *this* machine is box-fresh, and novelty has rekindled my crush. (You can see my *actual* laptop on page 43, where its design is praised as iconic.)

I love my MacBook Pro because its broad but slim body seems luxuriously solid yet also gracefully light. I love how the resistance subtly increases when I press a key, flattering my touch. I love the crisp definition of the graphics on its large, luminous screen. Most of all, I love how all my Macintosh software shares an elegant iconography and navigation scheme, and how all my Apple hardware works together uncomplainingly. The 17-inch MacBook Pro, in the famous phrase of Steve Jobs, Apple's founder and chief executive, is "insanely great."

The software application I am using is Microsoft Word. It is *not* beautiful. Above this document is a toolbar with more than 30 icons, many of whose meanings escape me. Above the toolbar are 12 pull-down menus, each with countless functions, and although I have been using Word as my principal professional tool for more than 13 years, I still don't know which functions can be found in which menus, because there are too many functions, arranged with too little logic. Everywhere, there are pullulating features, obscure jargon, and confusing organization.

What makes a machine beautiful? In this issue of *Technology Review*, we ask what makes for good industrial and interactive design in technology products. Editing these stories, and thinking about artifacts as different as the MacBook Pro and Word, has suggested some tentative answers to me.

One common answer is that technology design should be simple. Certainly, thoughtful designers disdain "feature bloat," in which business managers add more and more features to products in order to appeal to more markets. In "Different" *(p. 54)*, Daniel Turner's account of why Apple's products are so reliably well designed, Don Norman, who was vice president of advanced technology at Apple, says feature bloat is difficult to resist: "The hardest part of design ... is keeping features out." But keeping it simple can create the Palm, the BlackBerry, or the iPod.

Still, simplicity seems an insufficient explanation for good design. It's easier for some machines than others to be simple, because they have fewer functions. The Palm, BlackBerry, and iPod have beautiful designs, but they do only a few simple things, and their beauty was less laboriously achieved than that of the MacBook Pro, which allows its users to perform a wonderful variety of difficult tasks.

The truth, perhaps, is that well-designed machines, whether they have few or many functions, should be *minimally* complicated. That is, they should have no more functions than is reasonable given their form; every function should be no more complicated than it needs to be; and the way each function works should be intuitively easy to understand. As Albert Einstein may have said, "Make things as simple as possible, but not simpler."

For example, a well-designed multifunction mobile device like the Helio Ocean (whose conception, design, and development David Talbot describes in "Soul of a New Mobile Machine" on page 46) is complicated insofar as it can be used for talking and messaging, gaming and Web searching, social and geo-computing. But all these functions are socially and contextually appropriate. Individual functions—say, e-mail—have been stripped of features that would feel frustratingly extraneous on a small screen; and anyone could straightaway use the device who had never seen it before.

By contrast, Word is badly designed not because it is complicated but because it is needlessly complicated.

Our design issue describes a few other characteristics of good technology design: it generally derives from collaboration among people in diverse fields, who are nonetheless subject to the focus and discipline of a tasteful despot like Steve Jobs; at its best, it is genuinely innovative, pushing manufacturers and engineers to develop new processes and techniques; and so on.

All of this matters because technology, which was at first the hobby of enthusiasts and then the property of professionals, is today used by billions in their daily lives. The further triumph of technology depends on good design. When a technology becomes a consumer product, says Bill Moggridge, a cofounder of Ideo and designer of the GRiD Compass, the first laptop computer *(see Q&A, p. 30)*, "it's completely essential for success that the thing is enjoyable to use and easy to learn. It *fails* unless it is."

Write to me and tell me what you think good design is at jason.pontin@technologyreview.com. **Jason Pontin**

Spanish company PharmaMar searches the sea for new cancer drugs.

Spain’s Biotech Revolution

In the past five years, Spanish companies and institutions have sharply increased their focus on biotechnology, and the results —in new companies, new products, and new research centers—represent an important contribution to the growing international field. This is the sixth in an eight-part series highlighting new technologies in Spain and is produced by Technology Review, Inc.’s custom-publishing division in partnership with the Trade Commission of Spain.

In conversations about biotechnology in Spain, one word appears repeatedly: revolution. According to many in the field, huge changes are afoot in Spanish science today. Though the country has historically focused on producing quality scientific research and papers, the past five years have seen a dramatic increase in the launch of companies, the development of new research centers, and the transfer of top-quality technology into economic development.

Both the national and local governments have embraced the current European focus on developing a knowledge-based economy, one that creates companies—and income—from the ideas of its citizens. National and local governments have increased funding for research, created new research centers, and provided mechanisms to advance technology transfer. Though this focus is relatively new in Spain, the strong scientific environment has provided a rich medium for the rapid growth of biotechnology, which has seen intensive investment and development in the past five years. According to Genoma España, a government-funded organization that promotes genomic research and practical applications, half of all scientific research in Spain focuses on biomedicine.

PHOTO COURTESY OF PHARMAMAR

Starting Up

The seeds of the current revolution were planted at the National Center for Biotechnology (CNB in Spanish), located on the outskirts of Madrid. For the past 15 years, CNB has housed and promoted top-quality science while simultaneously focusing on technology transfer and spinoffs. Eleven companies so far have sprung from the CNB labs. At 720 researchers, CNB is the largest center of the National Research Council—and the first to focus so intensively on technology transfer. “For instance, we were the first center

to have our own technology-transfer office," says CNB's director, José Ramon Naranjo.

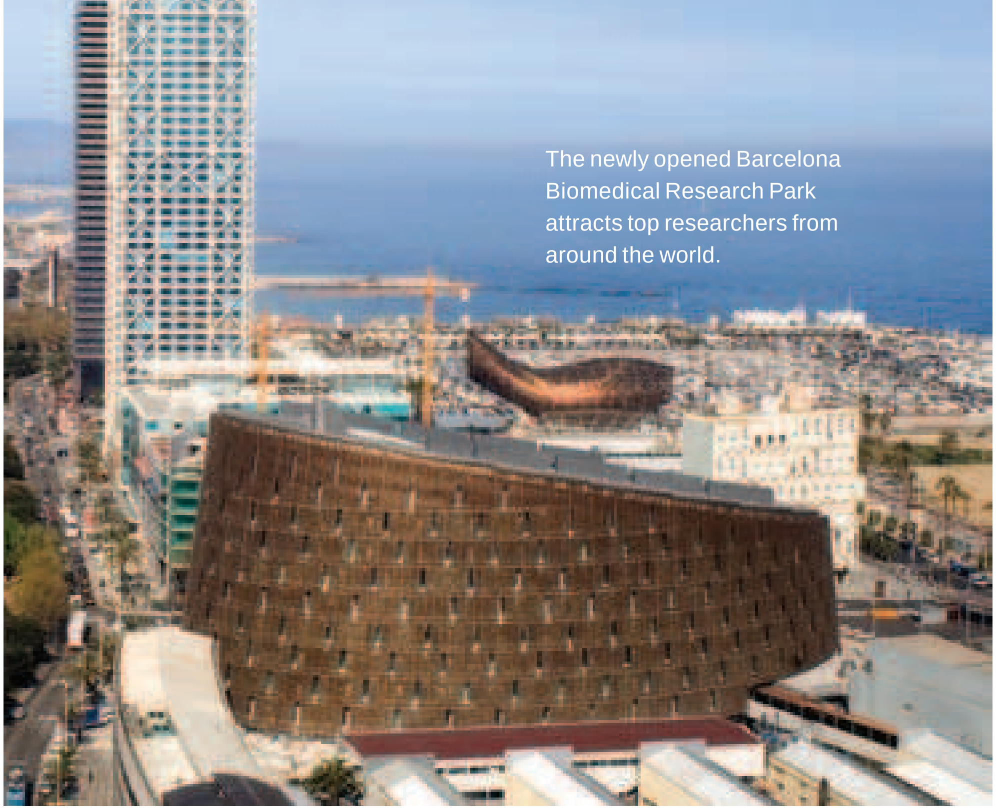
The departments cover a wide variety of topics: researching viruses and developing vaccination protocols; analyzing microorganisms for their potential in bioremediation; studying pathogens and their mechanisms of disease production in order to develop new antimicrobial compounds; studying species of wine grapes to understand how the plants produce defenses to cope with viral attacks or lack of nutrients.

One group at the center recently developed a method for studying the genome of a pathogenic salmonella strain (previously only a nonpathogenic strain had been studied) in order to better understand its virulence. Another company on-site is working on a landmine detection system based on the ability of certain bacteria to eat explosive compounds. These bacteria have been manipulated to glow at night if they are "happy," as Naranjo explains—"and they're happy when they're eating this compound."

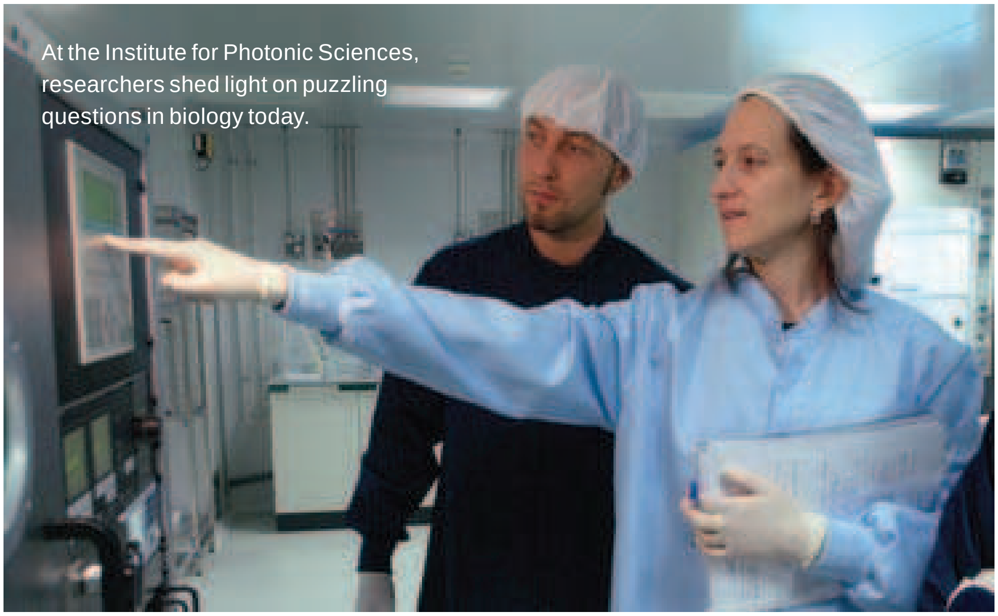
Though the salaries of researchers are paid by the Spanish government, the research itself is funded by grants from around the world. The center recently won a grant from the Bill and Melinda Gates Foundation for its work as part of a consortium developing an HIV vaccine.

This type of work is representative of much of the top biomedical and biotechnology research going on around the country. Spain has a strong background in research: the country has historically produced a significant percentage of the papers published in scientific journals from European research centers.

Manel Esteller, director of the Spanish National Cancer Center (CNIO in Spanish), is one of the first Spanish scientists to land on the pages of the *Wall Street Journal*. His research on monozygotic twins (who share the same DNA) and cancer, and how aging and environment affect DNA and the incidence of cancer, has broad implications for treatment and management of the disease.



The newly opened Barcelona Biomedical Research Park attracts top researchers from around the world.



At the Institute for Photonic Sciences, researchers shed light on puzzling questions in biology today.

BOTTOM PHOTO COURTESY OF ICFO-THE INSTITUTE OF PHOTONIC SCIENCES®; PICTURE BY LUIS MONTESDEOCA

TOP PHOTO COURTESY OF PRBB

The strength of Spanish research has drawn international companies to set up research facilities in the country. Pharmaceutical firms including Merck, Lilly, Abbott, and Baxter have developed labs in Spain. The French pharmaceutical company Sanofi-Aventis is currently investing nearly eight million euros (about $10.5 million) in a new basic-research center outside Madrid.

The CNB's focus on technology transfer had been historically rare in Spain. In the past, there had not been much interest in patenting discoveries, or in transferring knowledge to companies that could develop and market the resulting technologies and profit from the research.

"We've produced about 4 percent of papers on biotechnology in the world, and we're the fourth country in Europe in terms of those publications, but we've been at the back of the line in terms of patents," says José Luis Jorcano of Genoma España.

The organization primarily provides funding for major research programs, such as one, in conjunction with Genoma Canada, studying fish metabolism and changes in the expression of

genes at different points in fish development. This knowledge serves to better map fish development and ascertain what foods best meet fish needs and at what times—all for more efficient and effective aquaculture.

"We fund a number of genome projects studying plants, fish, and animals, because when you look at exports from Spain, a large portion of them are from agriculture," says Jorcano. Like CNB, Genoma España also provides funding and assistance for spinoffs.

But many of the organization's efforts have involved tracking the growth of the biotechnology sector over the years. There have been dramatic changes. In a recent study, Genoma compared Spain against other European countries, the United States, and Canada. After adjusting for population and income levels, the study found that though Spain's sector is still relatively small compared to the big international players, it is the fastest growing. In the last two years, the number of companies solely devoted to biotechnology has increased by 40 percent. On average, public and private investment in biotechnology is growing at 22 percent and 32 percent per year, respectively.

Bioincubators provide one method for promoting the growth of these new biotechnology companies. On the same campus as CNB, a bioincubator at the Madrid Science Park hosts companies in early stages of development.

The Madrid Science Park (PCM in Spanish) was created in 2001 to promote technology transfer from the academic to the private sector. "These types of parks here in Spain offer a new physical space to create better relationships between universities and companies," says its director, Antonio Díaz. There are already more than 45 companies in the park.

At the moment, eight biotechnology companies line PCM's halls. With only a few employees each, the companies share office and lab space and have access to expensive equipment that would usually be out of financial reach at this early stage. In addition, the arrangement provides them with administrative assistance in developing their businesses.

The most advanced research is led by Victor Rosas, head of Decantum Systems. Rosas has spent decades in academia developing a food safety test that quickly separates, for instance, fats and proteins in an animal's liver. The tests, which can also detect illegal substances, are significantly less expensive and exponentially faster than techniques used today in food safety. The company is already selling the first kits to a handful of regions in Spain before beginning to market them internationally.

"The types of science parks here in Spain offer a new physical space to create better relationships between universities and companies."

Another regional bioincubator officially kicked off in the Basque region five years ago. Actively promoting company creation, the local authorities set up new biotechnology research centers, with top-of-the-line facilities in genomics, structural biology, and many other related fields. Though the area does not have a long history in biological research, as is the case in Madrid and Barcelona, its rich history in engineering and manufacturing provides the basis for the government's recent push to expand into biology.

"We can use our know-how and expertise to create biosensors, or robotics and automation for biology, which is what some of the companies are involved in," says Maria Aguirre, head of BioBask, the government agency in charge of the effort. In the last four to five years, she adds, a new company has been created, on average, every three months. Sixty companies are already part of the initiative, and the Cooperative Research Center (CIC bioGUNE), a multidisciplinary center to advance research in biology and health, opened last year.

At the University of Navarra in Pamplona, a new project called the Center for Applied Medical Research (CIMA) pairs university research centers with an applied-pharmacology investigation center, a hospital with a department for clinical trials, and a private company to develop new products and bring them to market.

In all, Spain has about 25 functioning science and technology parks, with about 45 more in development—and literally thousands of companies working in a wide variety of scientific fields have been incubated in these parks or spun off from them. This model itself has become a Spanish export. Brazil, Chile, Mexico, Argentina, and some countries in Eastern Europe have expressed interest in creating similar centers.

New Bioregion

Though Madrid has traditionally been the center of gravity for Spanish scientific research, Barcelona today practically buzzes with energy about biomedical science. New research centers have sprung up around the city in the past few years. Investment in biomedical research continues to climb. There's a new focus on training professionals to deal with the details of technology transfer: filing patents, raising funds, running a business.

The organization Biocat, the BioRegion of Catalonia, was created as a way to formalize this effort; it's a government-funded umbrella organization that unites government, business, and academia to facilitate research, technology transfer, and business creation. "We realized that here in Catalonia, we're great at creating knowledge," says Manel Balcells, the president of Biocat. "But we need to improve in technology transfer, in taking that knowledge and converting it into economic value."

New scientific resources in the region have added both to the scientists' capabilities and to the excitement. The

fourth-most-powerful computer in the world—the most powerful one devoted entirely to science—is located near the Barcelona Science Park (PCB in Spanish). PCB is home to southern Europe's most powerful nuclear magnetic resonance imaging machine, which is used to determine molecular structure. And a new synchrotron—a sprawling, high-energy particle accelerator—is under construction just on the other side of Barcelona's mountains.

Much of the research done by Spanish pharmaceutical companies has historically been based in this city. Barcelona's hospitals conduct research in addition to providing care. And the universities have contributed to the base of knowledge about biological processes.

PCB, which is located on the University of Barcelona's campus near the city's fabled soccer stadium, opened in 2000. In addition to a number of research institutes on site, PCB also houses more than 30 companies in various stages of development, including three oncology labs of Merck Germany.

The largest of the on-site institutes is the Institute for Research in Biomedicine (IRB Barcelona). In one lab researching peptides and proteins, headed by Ernest Giralt, researchers are examining how different molecules "talk" to one another and how proteins recognize each other. The goal is to develop molecules that can prevent the development of certain diseases, such as Alzheimer's. Another team, headed by Antonio Zorzano, investigates antidiabetes compounds and examines the role of mitochondria in preventing disease.

"We are competing against the whole world," says Zorzano, "so what we have to do is try something new, not just research what's obvious. And we're very excited here at IRB Barcelona about where the science is going. In Spain we're no longer focusing just on publishing. It's about doing something else for society, and for the whole world."

That excitement was what drew Lluis Ribas de Pouplana back home to Spain, and to IRB Barcelona. He'd been in the United States at the Massachusetts Institute of Technology, then at the Scripps Research Institute in California. "One of the parameters for where I wanted to work was how easy it would be to start a spinoff," says Ribas de Pouplana. "Barcelona—and the IRB—seemed to be a great place to go." Ribas de Pouplana has developed a company to capitalize on his research, using human tissue samples to test drugs for positive characteristics rather than relying on time-consuming tests that individually knock out drugs on the basis of negative characteristics. This technology has the potential to dramatically shorten the time needed for testing pharmaceutical compounds.

The Barcelona Science Park and IRB Barcelona exemplify the growth in the region. The PhD program attracts international students, and scientists from different departments wander freely among the various labs, exchanging ideas, continuing research, and innovating. New buildings are under construction.

Across town, at the new Institute of Photonic Sciences, projects shed light on some challenging questions in biology today. One team, led by Dima Petrov, designs optical tweezers that can hold a cell in place, suspended in liquid, and then uses the same beam or a different laser source to perform chemical analyses of the cell. The result is a brightly colored visual display of the chemistry of a cell in situ. This novel technique can be useful in studying blood cells, which are best understood in suspension; it can help reveal, for example, the mechanism and location of drugs entering those cells.

Another team is at the early stages of using light to encourage neuron regrowth. "The problem is that neurons do not regenerate," says Pablo Loza-Alvarez, who heads the team. "If a neuron is broken, from a degenerative disease or from a spinal-cord accident, there's no way to repair it. We're at the very beginning of tackling this problem."

The team has demonstrated that neuron filopodia—the sensors at the end of the cell—will actually grow toward the pulse of a special laser. This is the first time this technique has been applied to live neural cells. "These are the beginning stages, but this approach is opening a completely new path of research that could help a lot of people," says Loza-Alvarez.

"We want to revolutionize biomedical research. When different disciplines get together, you create innovation."

In one of the most promising new technologies, Romain Quidant heads a team that uses light to provide the structure and power source for the elusive lab-on-a-chip. Light, focused by specific properties in gold, becomes strengthened and magnified. This strengthened light can serve to push molecules on a chip and trap molecules of certain sizes and shapes. This way, a solution could theoretically be broken up into different compounds. Then that same energy source, light, could be used to analyze the chemical components of the compounds.

"This small piece would include all the functionalities needed to perform, for example, an analysis of drugs or blood," says Quidant. "From a small quantity of liquid you could separate out different elements, manipulate them, analyze them, and do it all in parallel. This is something that could end up cheaper, faster, and more reliable."

By far the most visually arresting scientific building in Barcelona claims a prime location overlooking the beach along the city's Mediterranean coast. Opened in May 2006, the Barcelona Biomedical Research Park (PRBB in

PharmaMar researchers dive at sites around the world to collect samples.

At PharmaMar's labs, samples of sea life are tested for their ability to combat tumor growth.

Spanish) is the region's newest and largest facility devoted entirely to biomedicine.

The beachfront property has space for 1,000 scientists, making it among the largest research centers in Europe. More than 80 research groups attract scientists from around the world, covering topics such as bioinformatics, gene regulation, cell and developmental biology, and research on embryonic and adult stem cells. In fact, this center is the first in Spain to work with embryonic stem cells.

The building will also house clinical trials on-site, one unusual aspect of the research. "We believe it's good to make the basic scientists understand that there is time pressure," says Reimund Fickert, project director at PRBB. "We want the medical doctors to interact with them. They should know there are people dying, and that the basic research is related to a medical necessity."

Like the other new research centers, PRBB focuses on interdisciplinary research and encourages interaction among scientists. Says Fickert, "We want to revolutionize biomedical research. When different disciplines get together, you create innovation."

Answers from the Sea

In the lobby of PharmaMar, a biotechnology company on the outskirts of Madrid, neon fish dart through a coral-filled aquarium. On the walls hang dramatic photos of underwater creatures. These visuals highlight a relatively unexplored terrain in biomedical research: the sea. PharmaMar's research offers a tantalizing glimpse at this new frontier in medicine.

"Most of the drugs that have been a success in cancer treatment have come from a natural source, but a terrestrial source," says Carmen Cuevas, director of research and development for PharmaMar. "Why not use the sea as a source, if life started in the sea?"

This idea is exactly what spurred the creation of PharmaMar, one of Spain's oldest biotechnology companies, in 1986. Founder José María Fernández-Sousa, then a university professor involved in research and development at a local company focusing on microbiology and antibiotics, met a University of Illinois chemist who was examining marine products. Fernández-Sousa thought the sea could be a potentially perfect source of novel compounds, particularly those with antitumor properties.

Today, PharmaMar researchers organize six or seven expeditions a year at sites around the world, partnering with local research institutions in the host countries. Divers return to the surface with thousands of small samples of representative local marine life, though they're careful to avoid all endangered species; they have a strong company commitment to preserving the ocean environment. The result of these efforts is a library of frozen marine life under the building. With more than 42,000 samples, it is the largest such private library in the world.

Chunks of samples wait in smaller freezers in the labs at PharmaMar, filling the air with the tang of the sea. A scientist pulls out one dark-brown frozen lump and scans it into the computer: it's a sponge, and the photograph that appears on screen displays a significantly more attractive sight, with pale waving fronds fanning out. All samples are classified not only by species but also by the exact GPS location of the discovery site, with a visual description of the location and photographs of the species. This can assist

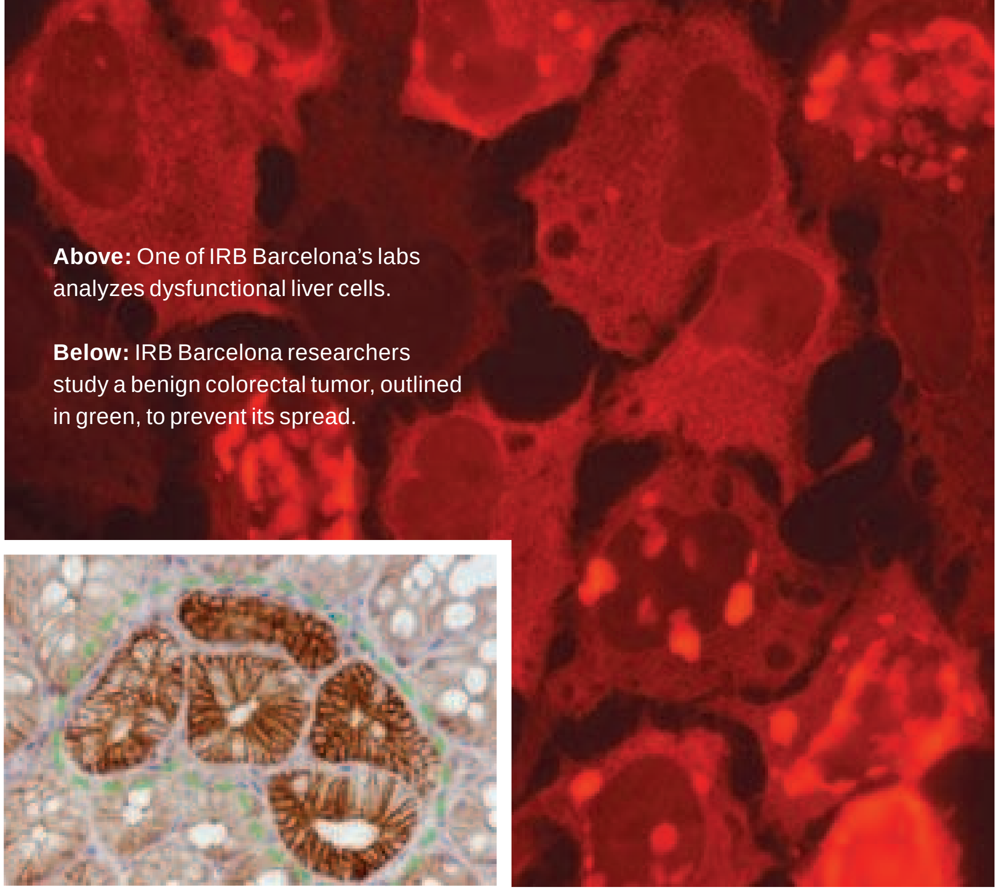
PHOTOS COURTESY OF PHARMAMAR

divers should they need to return to the site to collect further samples.

After the samples are scanned, small shavings are tested for antitumor properties. But the invertebrates aren't the only species tested; all the bacteria and fungi colonizing the creatures are cultured and tested as well. Scientists evaluate the potential of tens of thousands of samples each year. When one shows promise in combating tumor growth or killing tumor cells outright, the molecule responsible is isolated and patented, and then chemists develop synthetic versions of it. Those new compounds then begin the same drug-testing path as all other potential cancer drugs.

Today, the company has 250 employees working on all aspects of drug discovery, identification, synthesis, and testing. One compound, Yondelis, which is derived from a tunicate named *Ecteinascidia turbinata*, is close to receiving approval for treatment of soft-tissue sarcomas. Yondelis is also being studied for the treatment of ovarian, breast, and prostate cancer. Four other compounds are in earlier testing phases. And according to Cuevas, a handful more are promising, though she says it's too early to be specific.

"If we pass the European authorities and begin marketing the drug, this will be an important moment," says Cuevas. "It's important for the company, because it will be the first pharmacological drug that PharmaMar puts out on the market. It's important for the marine-science community, because it will be the first marine cancer drug on the market. And in general, it will show that this isn't a crazy idea, as people thought when Dr. Fernández-Sousa started. It will demonstrate that the sea can be an important source for new drugs."



Above: One of IRB Barcelona's labs analyzes dysfunctional liver cells.

Below: IRB Barcelona researchers study a benign colorectal tumor, outlined in green, to prevent its spread.

PHOTOS COURTESY OF IRB

Growing New Companies

Though Spain has a number of homegrown pharmaceutical companies, as well as a few companies formed in past decades that focus on biotechnology, the most significant increase in companies formed has taken place in only the last five years.

One of the most prominent examples of this new growth is Genetrix, formed by Cristina Garmendia (who also heads the Spanish biotech trade association ASEBIO). Genetrix spun off from the CNB in 2001, when Garmendia realized that while Spain produces a significant amount of quality research, there were limited paths to commercialization. She came to an agreement with the Spanish Research Council to buy a number of patents. The company began acquiring patents and building a base of widely varied services and research. Today, Genetrix has given rise to seven other spinoff companies.

"When I first joined, a year ago, we had 50 or 60 employees," says Claudia Jimenez, who is in charge of the company's corporate development. "We're already up to 100. And every month there are two or three new faces in the office."

In new labs being constructed for the spinoff Cellerix, the most advanced company in the Genetrix family, researchers walk around covered from head to toe in white, with white caps covering all exposed hair. They're preparing a new lab to work with adult stem cells. This is the only company in Spain with the authority to produce stem cells suitable for use in medicine.

Cellerix has two different lines of research. One, in clinical trials, uses stem cells from fat tissue commonly found in the abdominal region to treat complex perianal fistulas. There is currently no truly effective treatment for these fistulas, which occur when an opening forms between two passages in the body in the course of a variety of diseases, particularly Crohn's disease. "The only treatment today is surgery, and in most cases the fistula reappears after surgery," says Gabriel Marquez, vice president of research at Genetrix. "Plus, the surgeon almost always has to cut the sphincter muscles, so there's practically a 100 percent guarantee that the patient will suffer from incontinence."

In the treatment that Cellerix is studying, adult stem cells are isolated from the patient through liposuction, cultivated, and then implanted in the patient. In trials, this therapy has healed the ruptures. This is one of the most advanced studies using adult stem cells from easily obtained lipids (as opposed to bone marrow, for example) for therapeutic purposes.

A second line of Cellerix's research, also in clinical trials, is devoted to the rare skin disease epidermolysis bullosa, in which patients lack a critical protein.

Even slight contact can cause the patient to literally lose skin. The skin substitutes in use today are not transplants and must be periodically replaced. Cellerix is developing a transplant consisting of a mixture that includes cells from the patient's epidermis and cells from healthy, compatible donors. The company has already achieved clinical proof of concept.

Working with adult stem cells is so new that the Spanish government has had to develop new regulations for this type of research. Even among European regulators, such research raises questions. "We are one of the few companies in Europe working with adult stem cells," says Marquez, "so the EMEA, which is the European FDA, calls us to give our views on the research. The whole field is so new that even the regulators have to figure out how to regulate."

Another Genetrix company, Imbiosis, has developed a novel method for detecting gluten. This is important to food processors in marketing to patients with celiac disease, which makes them sensitive to gluten. The company Sensia is creating a small, easy-to-handle biosensor to detect tiny amounts of a given compound in the environment.

With a handful of years of experience in starting biotechnology companies, Genetrix is also becoming a service company, starting to offer professional assistance to outside startups in, for instance, patenting, business development, and human resources. And the company has created something of a buzz in the biotech world. "Now, people come to us from the academic world to tell us about their data," says Marquez. "They want to know if we're interested in licenses or patents, or helping them go ahead with preclinical testing. We've managed in recent years to create real credibility."

Developing Experience

Credibility is crucial in this emerging field. The company Advancell began when its university-based founders realized that their services in cell-based reagents were in high demand. Today the company has two main areas of operation: one in services and the other in innovative pharmaceutical products.

The pharmaceutical arm of the company is developing a new system for drug delivery based on nanoparticles and natural biopolymers. Basically, a naturally occurring substance called chitosan, a powder made of crushed crustaceans, provides the transport mechanism to encapsulate drugs in nanoparticles. This can be useful for topical delivery of drugs used to treat eye diseases, or for oral delivery of drugs such as insulin. Because this new technique is being tested with drugs that have already been approved, the trial phase is only about two years, as opposed to the usual 10 for testing new drugs—and these existing drugs could see dramatic improvement in efficacy and safety.

Advancell's business model is typical of many current Spanish biotech companies: they began providing services as a way to earn money and then invested that money in research and innovation.

The business model isn't the only typical feature of the Advancell story. CEO Luis Ruiz says his personal story reflects the experience of most others in the current generation of biotechnology entrepreneurs in Spain. He was a molecular biologist with years of experience in academia, then shifted to the local pharmaceutical industry and spent four years in business development.

"I had the rare hybrid academic and business profile that is required for managing these kinds of companies," says Ruiz.

Of other heads of companies that started within the past five years, such as Garmendia of Genetrix and Carlos Buesa of Oryzon Genomics, Ruiz says, "All of us came from the university, at a certain point shifted to industry, and with this experience began managing biotech companies."

Today the company has 30 employees. The services arm is already making money, and the research arm is closing in on creating a marketable product. "Now there are more people with a variety of experience," says Ruiz, but in 2000 or 2001, when the current generation of biotech business began, "not many people were willing to take the risk." Today, though, the field has changed. He adds, "I feel a little privileged; I'm a player in something that is evolving very positively, and I'm optimistic about where it's moving."

"I feel a little privileged; I'm a player in something that is evolving very positively, and I'm optimistic about where it's moving."

Challenges

As players in an emerging biotech market, Spanish companies still have some challenges ahead. The first and most significant one, many observers say, is access to financial resources. Spanish investors are only now beginning to understand the potential of biotechnology and make a long-term commitment. And those same Spanish investors are crucial in getting companies to a place where they will be attractive to international investors.

That's the position Cellerix, the Genetrix spinoff, has already reached. Genetrix is working on finding partners in Europe, Japan, and the United States. "When you turn to outside venture capitalists, they always want to have a Spanish local investor who takes the lead, and that's been difficult in the past," says Claudia Jimenez.

The small (though growing) amount of funds available for new companies means that many are underfunded, according to Alec Mian, the CEO of Genmedica in Barcelona.

Mian, a Canadian who ran a biotech company in Cambridge, MA, for eight

years, had been living in Barcelona and was considering moving to London to head another biotech company when he was contacted by Antonio Zorzano at the IRB to head a company based on Zorzano's research into an oral replacement for insulin.

This was a high-risk project, but "if successful, such a discovery and development would put Barcelona on the international biotechnology map," says Mian. "So even though the risk of the compound was high ... I decided to stay and give it a shot."

Another bottleneck is "how you manage the knowledge, more than in the creation of the knowledge," according to Luis Ruiz of Advancell. "We've already learned a lot, and we all have more experience now."

Joan Guinovart, director of IRB Barcelona, takes the management issue one step further. "We don't yet have any biotech millionaires," he says. "I think that would be a good incentive" to young scientists and business entrepreneurs starting out in biotechnology.

Taking on the Challenges

Despite the challenges in accessing investment, funding opportunities for biotechnology companies have increased dramatically in recent years as venture capitalists in Spain have learned more about the sector, and as companies start to mature and attract investment from outside the country. Many companies describe recent large-scale investments from Europe.

Genetrix is initiating the first venture capital fund specializing in biomedicine, named Vanguardia BioFund 1. It expects to fund startups and expanding companies, with about 70 percent of the investments to flow to Spanish companies.

In terms of management, the latest crop of CEOs now have years of experience and are beginning to bring their know-how to a new generation of startups. In addition, the infrastructure to support technology transfer is growing ever stronger thanks to government, academic, and industry commitment, both on a national and a regional level.

The change in the last five years illustrates this growth. Guinovart is one example. Ten years ago he patented a potential antiobesity drug—and licensed it to Bayer. The drug is now in phase II clinical trials. "Now it's the other way around," he says. "You try to exploit the patent yourself."

PRBB in Barcelona is tackling many issues in business skills development with a devotion nearly equal to its focus on world-class scientific research. "We're focusing on developing companies in the future, but first, the most important [thing] is to have the best science," says project director Reimund Fickert. To develop the knowledge base in the region about issues related to patents, finances, management, and similar issues, the research park has developed a series of executive courses geared to biotech executives and managers, venture capitalists, business students, and others. The courses attract lecturers from the top ranks of biotechnology around the world; for three days at a time, the programs provide a combination of serious education and equally serious networking.

The Spanish government has demonstrated its commitment to technology transfer through Ingenio 2010, a program that includes more than $1 billion in grant money for research and for efforts to encourage collaboration between the public and private sectors.

Spanish pharmaceutical companies are joining together to advance the industry. Zeltia, Rovi, Faes Farma, Lipotec, and Dendrico have formed an alliance and a common investigation project called Consorcio Nanofarma, a multidisciplinary research project on nanomedicine and drug delivery systems.

The rapid growth of the industry, coupled with the investment in world-class research centers, has increasingly called Spanish researchers home from around the world to contribute to the country's, and the world's, focus on the next wave of biotechnology.

Resources

ICEX (Spanish Institute for Foreign Trade)
www.us.spainbusiness.com

ASEBIO (Spanish Association of Biotechnological Companies)
www.asebio.es

Barcelona Biomedical Research Park (PRBB)
www.prbb.org

BioBask (Basque Plan for the Development of Biosciences)
www.biobask.org

Genetrix
www.genetrix.es

Genoma España (Foundation for the Advancement in the Research of Genomics and Proteomics)
www.gen-es.org

National Biotechnology Center (CNB)
www.cnb.uam.es

PharmaMar
www.pharmamar.com

To find out more about new technologies in Spain, visit:
www.technologyreview.com/spain/biotech

For more information visit:
www.us.spainbusiness.com

Contact:
Mr. Enrique Alejo
Trade Commission of Spain
in Chicago
500 N. Michigan Ave., Suite 1500
Chicago, IL 60611, USA
T: 312 644 1154 • F: 312 527 5531
chicago@mcx.es

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Forward

MATERIALS

Cheaper Diagnostics

By simultaneously scanning for thousands of genes or proteins in a biological sample, doctors could diagnose many diseases in a single step. But today's DNA or protein microarrays are too expensive for widespread clinical use, in part because their manufacture is a complex, multistep process.

A potentially cheaper tool for detecting telltale DNA and proteins appears on this page: capsule-shaped polymer particles, each 180 micrometers long. Each particle can be loaded with a specific biomolecule so that one half of the particle fluoresces when it detects a disease target. Imprinted with bar-code-like patterns of holes, the particles can be read optically; they could serve as detectors for more than a million distinct biological targets. Technicians with the right optical equipment could, in theory, mix the particles with a sample and read off the results.

Unlike microarrays, the particles can be manufactured using a single, integrated process, which was developed by MIT chemical engineer Patrick Doyle, doctoral student Daniel Pregibon, and colleagues at MIT and Harvard Medical School. The process begins with two adjacent 100-micrometer-wide streams of fluid. One of the streams contains biomolecules that will attach to disease targets. A pulse of ultraviolet light passes through a stencil and strikes the streams, causing precursors of polyethylene glycol in both to solidify into a single particle. The stencil gives one half of each particle an identifying pattern of holes.

Jay Groves, a chemist at the University of California, Berkeley, calls the synthesis a "clever" step toward low-cost diagnostics. One remaining challenge is to develop a more practical system for reading the particles: Doyle and colleagues use a bulky, impractical fluorescence microscope.

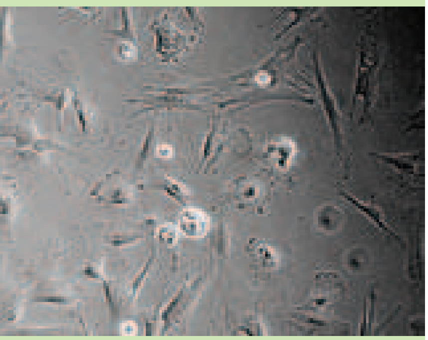
Peter Fairley

DANIEL PREGIBON AND PATRICK S. DOYLE

TISSUE ENGINEERING

Healing Bone with Stem Cells

For treatment of severe fractures, stem cells derived from bone marrow could be used to generate new bone tissue. But scientists need better ways to keep the cells alive once they're implanted. Linda Griffith and colleagues at MIT have created a new tissue-engineering material that could fit the bill. The comblike material consists of a Plexiglas backbone studded with molecular tethers that can attach to a specific kind of growth factor, a protein that helps many cells,



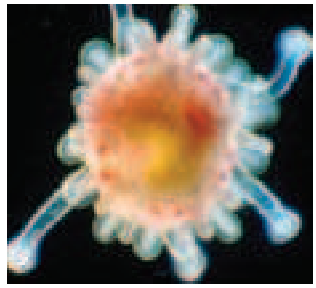
including stem cells, grow and differentiate. Adult stem cells grown on these scaffolds *(above)* were better able to survive and proliferate, potentially increasing the number of cells available to make new bone after transplantation. Scientists are now testing the material in animals. Griffith is planning additional experiments with human stem cells, to explore how tethering different proteins to the scaffold might do a better job of encouraging the cells to differentiate into bone. "We want to figure out, step by step, how to use marrow more effectively in the clinic," she says. —*Emily Singer*

CLIMATE CHANGE

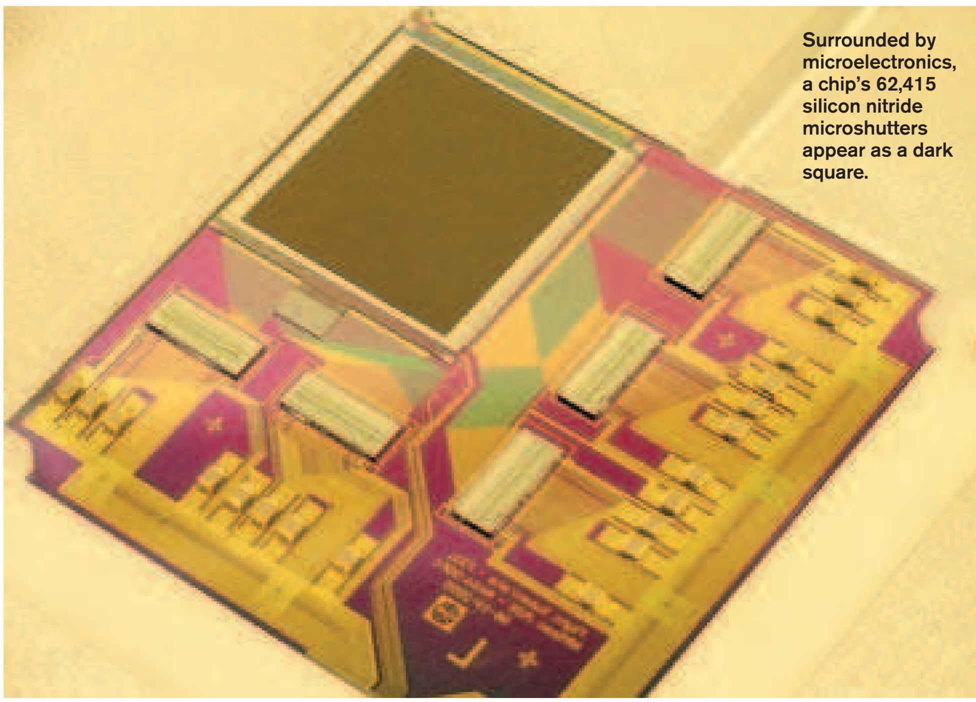
An Ocean of Worry

Can sea urchins survive the greenhouse effect? Using genetic analysis to determine how marine organisms respond to warmer and more acidic oceans, Gretchen Hofmann, a University of California, Santa Barbara, marine biologist, is finding troubling indications that the answer may be no.

After growing urchins *(right)* in conditions that mimic possible future climates, Hofmann's group studied select sequences of DNA to determine which of the urchins' genes had been activated in response to their environment. Hofmann focused on heat-shock proteins, which help stressed organisms repair other proteins. Early results show that the proteins work fine when urchins are confronted by warming water, but not when they also face the acidification caused by



even modest increases in carbon dioxide—suggesting that urchins may have trouble adapting. Hofmann has built a DNA microarray specific to urchins in order to study genetic effects of climate change in greater detail. **Emily Singer**



Surrounded by microelectronics, a chip's 62,415 silicon nitride microshutters appear as a dark square.

OPTICS

Micromachines and the Cosmos

Understanding the formation of the universe requires scrutinizing very faint infrared signals that tend to be overwhelmed by nearer, brighter light sources. Now, engineers at NASA Goddard Space Flight Center have designed a light filter with 62,415 micrometer-scale shutters that allows scientists to select the objects they wish to study and block everything else. The shutters are made of silicon nitride, and any one or hundreds of them can be opened or closed by a magnet and electronics controlled by a computer system that encodes a digital map of the cosmos. The microshutter system will sit atop a camera, called the Near Infrared Spectrograph, as part of the James Webb Space Telescope destined for launch in 2013. —*Brittany Sauser*

GERARDO AMADOR (OCEAN); COURTESY OF LINDA GRIFFITH (BONE); COURTESY NASA GODDARD SPACE FLIGHT CENTER (MICRO)

Dye spots on a sheet of paper form distinctive color patterns when exposed to the breath of lung-cancer patients.

DIAGNOSTICS

Lung-Cancer Breathalyzer

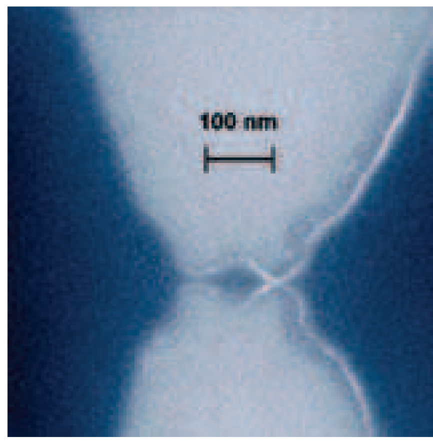
There was a time when doctors would sniff the breath of patients, looking for a yeasty note characteristic of tuberculosis or a sweet smell indicative of diabetes. Now researchers at the Cleveland Clinic could update olfactory diagnostics with a prototype breath detector for lung cancer.

Scientists have long known that cancer cells make distinctive metabolic products, called volatile organic compounds, that are exhaled. The differences between these compounds and ones exhaled by a healthy person can be detected using a combination of gas chromatography and mass spectrometry. But Peter Mazzone, a pulmonologist at the Cleveland Clinic, is working on a cheaper approach: a disposable piece of paper with 36 chemically sensitive dye spots. When exposed to a patient's breath, the spots change color; a computer then scans them for a telltale color signature. After tests involving 143 people, some with cancer and some without, the researchers found a color signature characteristic of three out of four actual lung-cancer patients. To hone the system's accuracy, they are now trying to identify the compounds exhaled by lung patients. With lung cancer killing 160,000 people each year in the U.S., technologies better than CT scans and dangerous needle biopsies are desperately needed. **Katherine Bourzac**

NANOELECTRONICS

Atom-Thick Transistor

Researchers at the University of Manchester in England have made a single-electron transistor using graphene, a sheet of graphite only one atom thick. Andre Geim, the professor of physics who led the work, says the transistor consists of electrical contacts *(blue areas at left and right, below)* that supply and collect current through three-nanometer-wide areas



(center) containing a central island of graphene, called a quantum dot. When current is applied, an electron jumps from one contact to the quantum dot and then to the other contact. A problem with previous single-electron transistors, says Geim, is that quantum dots of other materials, when shrunk this much, act "like a droplet of liquid on a hot plate" at room temperature. Graphene quantum dots, however, are stable. The Manchester research could yield a practical technology if fabrication techniques advance enough to produce such small features. *—Kate Greene*

LEONID PONOMARENKO (TRANSISTOR); CHRISTOPHER HARTING (CANCER)

Forward

MATERIALS

Good-Bye, Glare

Reflections can be a problem for optical technologies, limiting the amount of light absorbed by solar cells or emitted by LEDs. But a new nano coating that virtually eliminates reflections could make such devices more efficient. An LED, say, could emit 40 percent more light, leading to brighter displays. The image at right shows light reflecting from uncoated *(top three objects)* and coated materials. The second object from the bottom, a piece of semiconductor material used in LEDs, reflects 12 percent of light without the coating. The same semiconductor with the coating *(bottom)* reflects just 0.1 percent.

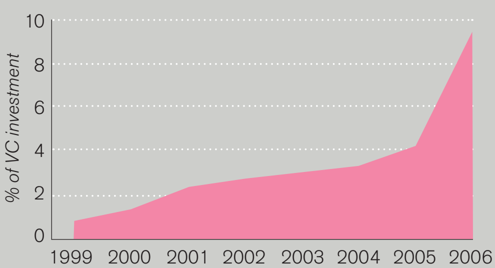
Reflectivity is related to the difference between the extent to which two substances, such as air and glass, refract or bend light. Reducing that difference reduces reflection where the materials meet. Researchers at Rensselaer Polytechnic Institute in Troy, NY, and semiconductor maker Crystal IS in Green Island, NY, created a multilayered, porous coating that eases the transition as light moves from the air into a solid material or into the air from a semiconductor in an LED. Each layer is made of nanorods grown at a precise angle. Successive layers bend light more as it moves into a solar cell. Likewise, light emerging from an LED is bent less in each successive layer. Products could be available in three to five years.

Kevin Bullis

VENTURE CAPITAL

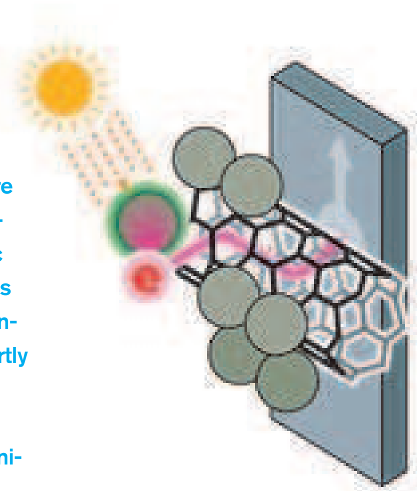
The New New Thing Is Clean Energy

Venture capitalists are starting to treat energy technology companies like the dot coms of 1999. The percentage of total U.S. VC investment devoted to cleaner-energy companies has been steadily rising, but it shot up in 2006, when $2.4 billion went to investments in companies involved in everything from ethanol production to photovoltaics manufacture.



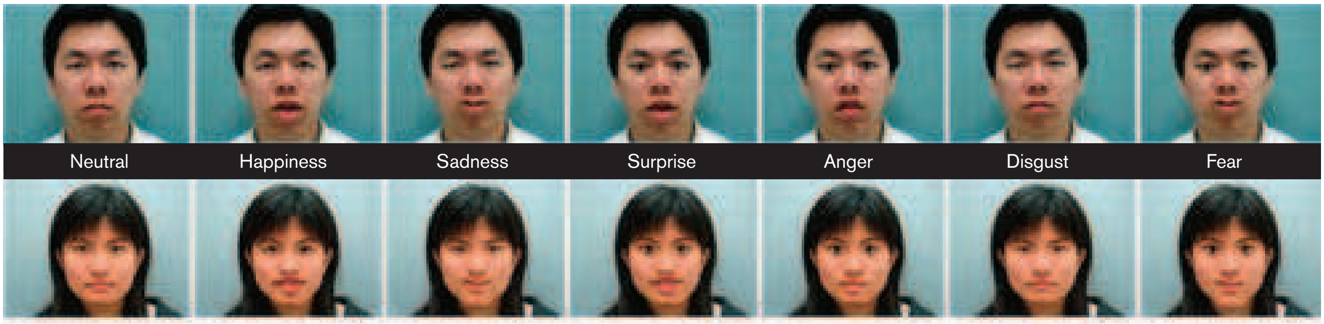
SOLAR POWER

Nano Solution



Nanoparticles show promise as an ingredient in solar cells, where they could absorb light and generate electrons. But photovoltaic devices made from nanoparticles are still far less efficient than conventional silicon cells. This is partly because some of the liberated electrons never reach an electrode. Now researchers at the University of Notre Dame in Indiana have doubled the efficiency with which these cells convert ultraviolet light to electricity. They deposited single-walled carbon nanotubes on an electrode to form a scaffold for electron-generating titanium dioxide particles. A carbon nanotube *(cylindrical object, above)* collects an electron *(shown in pink)* and provides a more direct route from the nanoparticles *(round objects)* to the electrode *(right)*. The cells convert ultraviolet light to electrons more efficiently than commercial silicon cells, but they do not yet work with visible light. *—Kevin Bullis*

JONG KYU KIM AND E. FRED SCHUBERT (GLARE); JEFF WEST (NANO)



SOFTWARE

New Face for Emoticons

E-mailers and text messagers may eventually use their own faces as emoticons, those ubiquitous combinations of symbols that represent smiles, frowns, and other expressions. In the photos above, the far-left images are the originals; the rest are products of software codeveloped by Xin Li, a Google software engineer who worked on the technology while earning his PhD at the University of Pittsburgh. Li's technology stores the neutral face—and the face-warping software—on the recipient's phone. When a messenger keys in text symbols—such as :) for a smile—the neutral face assumes the appropriate (well, sort of) expression. Since no photo is sent, the technology requires little bandwidth. It is finding its first application in virtual classrooms.

—Duncan Graham-Rowe

MEDICINE

Finding Surprising Drug Synergy

Someday, diabetics might be able to avoid insulin injections by taking an unlikely combination of an anticholesterol drug and a pain medication to control blood sugar. CombinatoRx of Cambridge, MA, has eight such counterintuitive but synergistic drug combinations in clinical trials, including the examples listed below. The company tests combinations of several thousand drugs at several different doses on cellular models of diseases. The reasons for the synergies are poorly understood; disparate drugs may act on the same molecular pathways.

—Katherine Bourzac

Drug combination	Disease target	Stage
Anticholesterol drug and analgesic	Type 2 diabetes	Entering phase II clinical trials this year
Antidepressant and cardiovascular drug	Rheumatoid arthritis	Results from preliminary phase II trials expected this year
Steroid and antiplatelet drug	Rheumatoid arthritis, osteoarthritis	Phase II clinical trials will finish in 2008
Steroid and antidepressant	Chronic lower-back pain, asthma	Phase II clinical trials will finish in late 2008

INTERFACES

Messy PCs

For those who prefer messes, there's now a program that turns the PC desktop into the equivalent of the paper-strewn office. Abandoning folders within folders, the new approach, called BumpTop, uses paperlike icons that can be scattered, stacked, or stuck to virtual walls. The brainchild of Anand Agarawala, a former computer science graduate student at the University of Toronto, BumpTop borrows animation techniques from video-game development, and the icons move as if they were subject to real gravity, momentum, and friction. "The 'PC desktop' was supposed to be a metaphor for managing our files," says Agarawala. "But my real desk looks nothing like my desktop." He has cofounded a startup in Toronto to commercialize his technology. **Wade Roush**

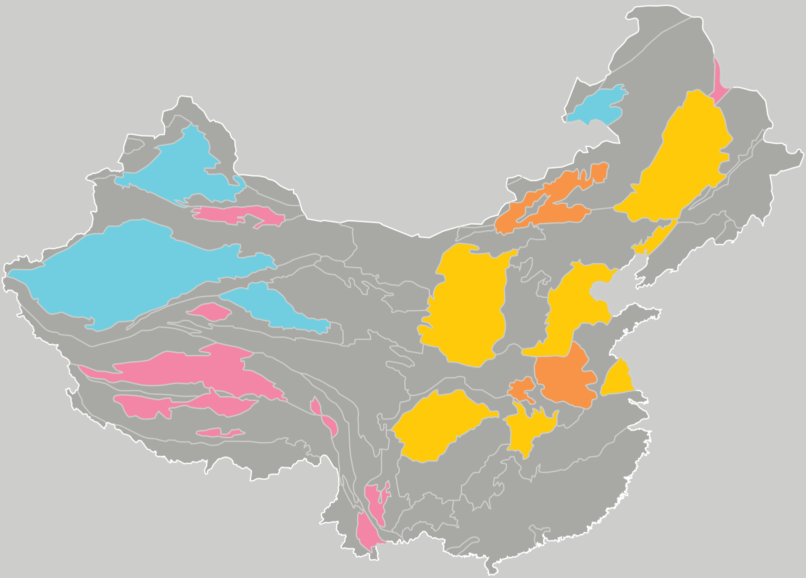
CHIEH-CHIH CHANG, SHI-KUO CHANG, AND XIN LI (FACE); ANAND AGARAWALA (MESSY)

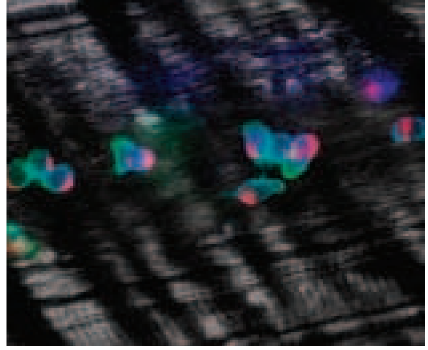

REVOLUTIONIZING
GLOBAL RECONNAISSANCE
The National Reconnaissance Office Director's Innovation Initiative (DII) Program nurtures innovative concepts and creative ideas. The program funds the brightest minds, best ideas, and break through technology from individuals in industry, academia, national laboratories, and the U.S. government. Log onto the DII website for proposal guidance, frequently asked questions, history, and BAA and GSSA requirements.
DII research funding supports cutting-edge scientific research in a high-risk, high-payoff environment.
• Innovation and Creativity
• New and Unique Ideas
NATIONAL RECONNAISSANCE OFFICE
UNITED STATES OF AMERICA
http://dii5.westfields.net

ENERGY

Coal Reality Check

Coal, the most abundant fossil fuel, is also the worst emitter of carbon dioxide, watt for watt. Coal burning generates 41 percent of the world's carbon dioxide emissions from energy use. And coal use is projected to rise steeply *(see "China's Coal Future," January/February 2007)*. A new MIT report—*The Future of Coal: Options for a Carbon-Constrained World*—describes a variety of advanced coal technologies but recommends that they be accompanied by technologies to capture and sequester carbon dioxide on a staggering scale. There "do not appear to be unresolvable open technical issues" surrounding feasibility and safety of sequestration, the report says; any hurdles "appear manageable and surmountable." The report contains suggestions about where the U.S. and China might begin putting all the carbon dioxide; in China's case, prospective storage areas *(below)* are ranked in order of priority for study. All are sedimentary basins; their ranking is based on geologic complexity and proximity to carbon dioxide sources. Yellow is highest priority, followed by orange, blue, and pink. *—David Talbot*





MEDICINE

Spying on White Cells

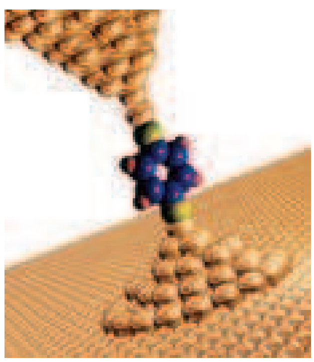
This image of the white blood cells of a live mouse is among the first to depict a process believed to play a role in sickle-cell anemia, in which deformed red blood cells starve tissues of oxygen. The misshapen cells can attach to larger white cells, worsening clogging in small blood vessels. Visualizations of this process could help researchers identify new molecular targets for drugs to relieve the painful symptoms of the disease, which afflicts 72,000 Americans and millions more globally.

In the image, made at Mt. Sinai Medical Center in New York City, three different fluorescent-tagged antibodies on the surface of white blood cells glow blue, red, and green, revealing distinct surface areas. A clearer view of the cells will help researchers identify the mechanisms by which sickle-shaped red cells attach to them, aiding the discovery of better drug targets. **Michael Gibson**

MATERIALS

Electricity from Heat

Materials that convert heat directly into electricity have been useful for some niche applications, like powering deep-space probes. But they've been too expensive and inefficient for their potential killer app: harvesting immense amounts of energy from the waste heat generated by power plants and cars. Now researchers at the University of California, Berkeley, have shown that a cheap organic material can make electricity from heat, potentially opening the way to affordable "thermoelectrics." The researchers trapped a few organic molecules *(represented by the multicolored spheres, above)* between a sheet of gold *(bottom)* and the ultrasharp gold tip of a scanning tunneling microscope. They heated the gold surface and used the microscope tip to measure the voltage created by the junction of molecule and metal. A large-scale heat-conversion system will require a process for arranging multiple layers of such junctions between two sheets of metal, one for applying heat and the other for harvesting electricity. *—Kevin Bullis*



ELAINE CHIANG AND PAUL FRENETTE (CELL); CAROL ZUBER-MALLISON (COAL); IMAGE BY BEN UTLEY, COURTESY OF ARUN MAJUMDAR (HEAT)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The Apple I

A look at Steve Wozniak's mother of all Apple motherboards.

By Daniel Turner

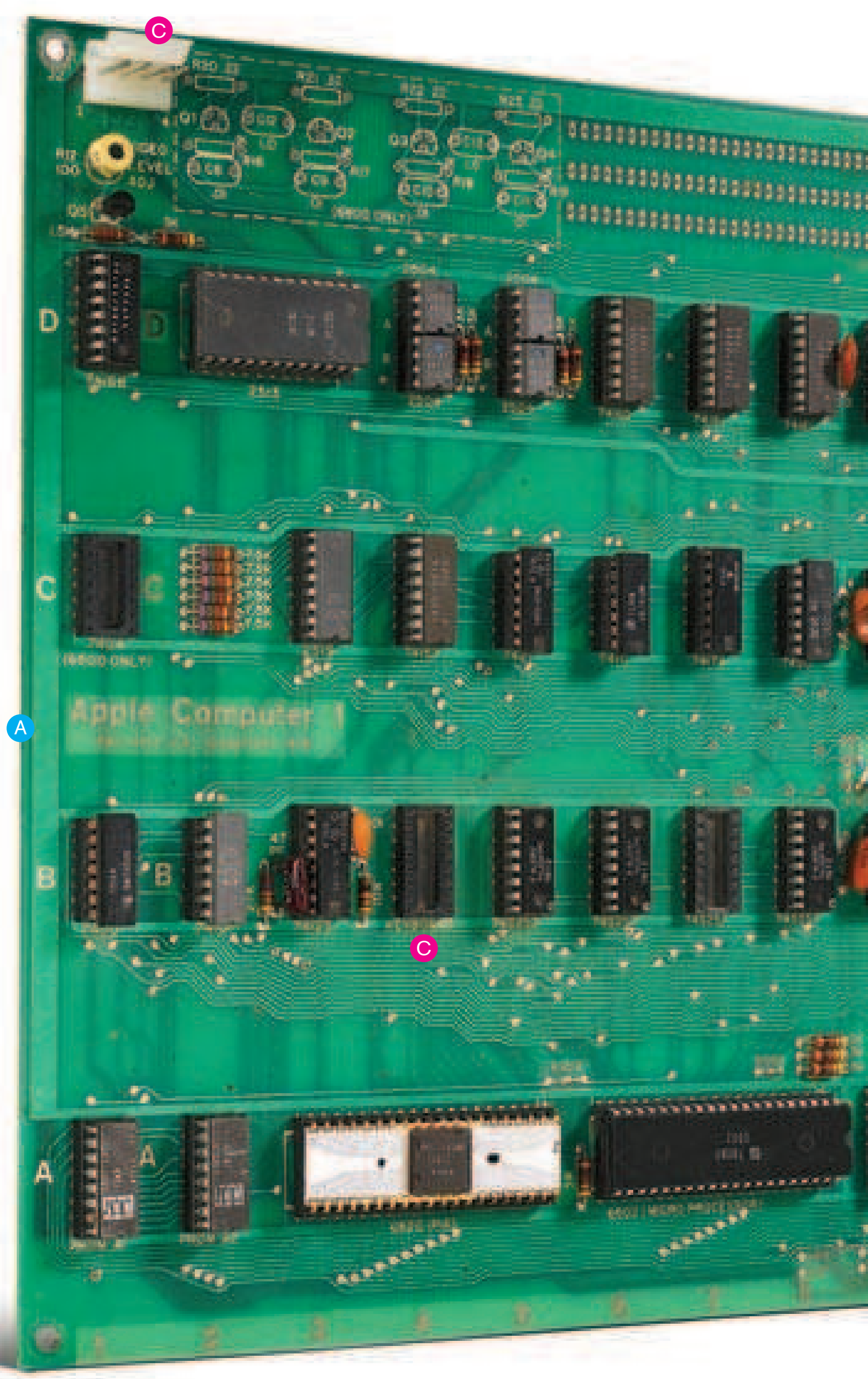
Before the iPod, the Macintosh, or even the formation of Apple Computer Company on April Fool's Day 1976, there was the Apple I. Designed by Steve "Woz" Wozniak, then an engineer at Hewlett-Packard, it was less a personal computer than the bare essentials of one: the circuit board you see here *is* the Apple I (buyers had to hook up their own keyboards, displays, and power supplies). This computer, the very first Apple I made, was first used in a math class at Windsor Junior High School in Windsor, CA, in 1976 and donated to the LO*OP Center, a nonprofit educational organization run by Liza Loop. In total, only about 200 of the Apple I motherboards were made. In 1977, Apple introduced the groundbreaking Apple II—which could be bought simply as a motherboard or assembled with case, keyboard, and power supply.

A Single-Board Design

Most microcomputers at the time used multiple circuit boards: one for the CPU, one for the video interface, one for the memory, and so on. "Woz took all the constituent parts of a microcomputer and put them all on one board," says Sellam Ismail, the proprietor of VintageTech, which maintains an archive of computer artifacts and history. Not only did this make construction cheaper and reduce power consumption, but it allowed users to build compact, all-in-one enclosures for the Apple I, leading to the unified design of the Apple II and the original Mac.

B Dynamic RAM

The Apple I shipped with four kilobytes of dynamic RAM (an extra four kilobytes was a $120 option). At the time, most microcomputers relied on static RAM, which was simpler to design for but more expensive than dynamic RAM. Wozniak devised an innovative, sophisticated circuit for the Apple I that enabled him to use the smaller—and cheaper—dynamic RAM chips.

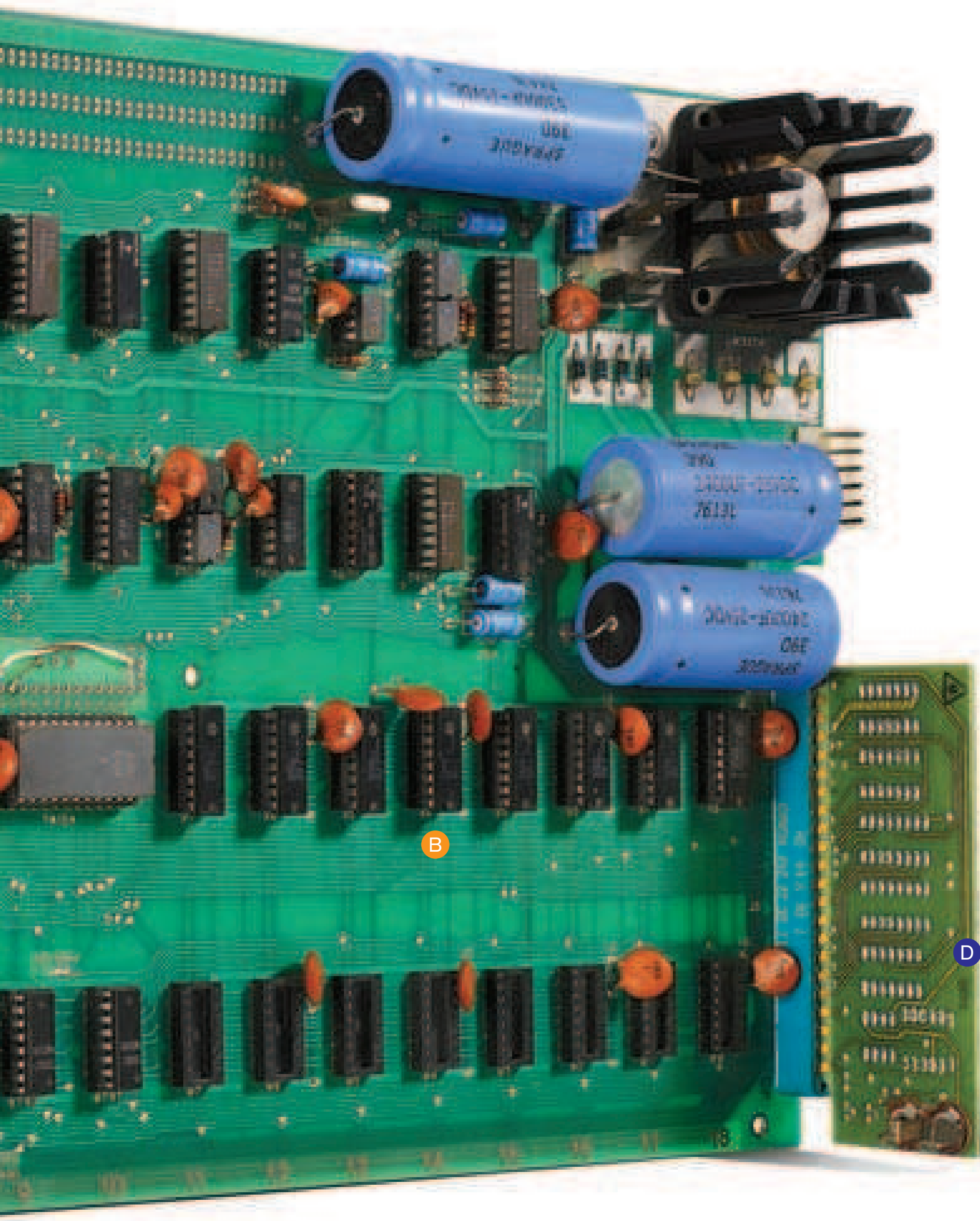


C Video and Keyboard Interfaces

At the time, many microcomputers relied for input and output on manual switches or electromechanical typewriters called teletypes. Wozniak built video and keyboard interfaces right onto the circuit board so users could "avoid all the expense, noise and maintenance associated with a teletype," in the words of one of the first Apple I advertisements. Bruce Damer, the curator of the DigiBarn Computer Museum in California, points out that although contemporary mainframes had cathode-ray-tube monitors, and Xerox's Palo Alto Research Center "was running networks of the revolutionary Alto computer, which used a mouse, windows, and icons," the Apple I could be connected to a standard TV set, making it seem far more accessible—or personal.

Low Cost as a Design Priority

"Woz liked the challenge of doing more with less," says Damer. Wozniak pored over integrated-circuit specifications and engineered the Apple I so that different processes could share the same chips, reducing the overall part count. This, plus the use of cheaper items such as a $20 MOS Technology 6502 microprocessor rather than the more common $175 Motorola 6800, enabled him and Steve Jobs to offer the Apple I for the somewhat affordable price of $666.66 ("Woz liked repeating numbers," says Damer), about $2,400 in today's dollars. According to Damer, "Woz was a total idealist—he wanted everyone to have access to computers." Loop, who is also the director of the History of Computing in Learning and Education Project, agrees: "Woz wanted this simple, low-cost design so that the Apple would be affordable for students and teachers."



D Cassette Interface

Early Apple I prototypes had no way to store data such as programs (they needed to be typed in every time you turned on the microcomputer), so Jobs and Wozniak soon added a cassette interface. This method of storing data, a precursor to the floppy disk and CD-ROM, already existed in the microcomputer market, but Wozniak created a design that used fewer chips and less power, cost less, and offered a higher data transmission speed. "Classic Woz," says Damer.

PETER BELANGER

Bill Moggridge

What makes for good design

Bill Moggridge has been an industrial designer for 40 years. In 1979, he designed what many call the first laptop computer: the GRiD Compass, which was used by businesspeople as well as by NASA and the U.S. military. The Compass established the language of laptop design: hinged closure, flat display, low-profile keyboard, and metal housing. In 1991, Moggridge cofounded Ideo, a design consultancy based in Palo Alto, CA. He is the founder of a movement known as "interaction design," which aims to do for the virtual world what industrial design does for the physical. In the recently published book *Designing Interactions*, he interviews 42 influential designers.

***TR:* You say that at the beginning of any design, two things matter most: people and prototypes. Why?**

Moggridge: What we're looking for is the latent user needs in a situation where, at least at the beginning, you don't know what you're going to be making. So you have to have insights about people driven from *their* psychology, *their* desires, *their* interests, and then apply that to the context where you might be inventing or coming up with a solution for a new product or service or space, or whatever the context may be. Once you've got to a first prototype, build it quick and try it out. As soon as possible—even a small attribute of it—try it out, because you're likely to be wrong.

Do companies get this more now than they did 10 or 15 years ago?

Oh, definitely, yes. The whole idea of design and design thinking is becoming much more recognized as an essential element for success. Industrial design was seen as important in the early years of mass-produced consumer products in the U.S.A. In the 1940s and 1950s, everywhere else that was in an advanced stage of development was suffering from the aftereffects of the Second World War and just trying to put bread on their table, whereas in America, it was a stimulus. And the result was that we had a consumer society in the 1950s. At that time, designers like Raymond Loewy [who designed everything from the Lucky Strike logo to the Studebaker Avanti to the inside of the *Saturn V*] made a big contribution as innovators. And then the business leaders thought, Okay, it's cheaper if we build an internal industrial-design department instead of using consultants, but they usually buried it in the R&D department, reporting to midlevel engineering. So American design got lost and only came back relatively recently, in the last 15 years.

How can tech companies better understand the needs of customers?

They should always be looking at what people are doing and why they want things. In my book, David Liddle [a Xerox PARC alumnus and user-interface pioneer] explains that there are three phases of adoption for a piece of technology: enthusiast, professional, and consumer. There comes a point where an industry realizes that the enthusiast phase could be applied for work. And then they start designing products which make us more productive. We're actually quite willing to learn something that's difficult to use and not very enjoyable if it makes us more productive. Then, finally, that technology becomes less expensive and more obviously applicable to our daily lives, and then people realize, Well, there could be a consumer product. And then suddenly, it's completely essential for success that the thing is enjoyable to use and easy to learn. It *fails* unless it is.

Why did it take so long for something as physically beautiful as the iPod to come about?

When I went to my first Hanover Fair in 1972 in Germany and went into this enormous place—22 halls they had, which included computers—I was just blown away by the excellence and the beautiful wonder of these machines. Companies like Nixdorf from Germany and Datasaab from Sweden were doing just stellar designs that seemed to be really inspirational. Then it seemed that we kind of stepped way back. We lost our ability to be doing interesting things in computers for a long time.

Why?

Well, I think maybe it just moved into the mainstream professional phase. In the early days, they were more driven by prestige, probably.

What's a good example of stellar design today?

The iPod. And it's going to be interesting to see what happens with the iPhone. I haven't had a chance to play with that. All you can tell at this point is that it's a stunning visual design. But whether it's going to be important, influential, successful—all those things are yet to be discovered. It's a much more challenging task to move into the telephone world now than it was to be at the leading edge of the iPod world.

Parting advice?

Put together a team with a great engineer, a crazy designer, a good businessperson, and a good human-factors scientist or psychologist of some kind, and put them in a room and get them to try to work together. It's a big challenge, but they come to a point, surprisingly quickly, where they realize that what they can achieve together is much more than they could do individually. **NATE NICKERSON**

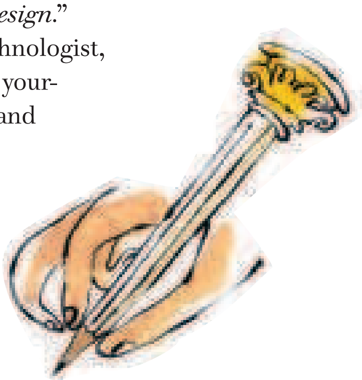
HOWARD CAO

DESIGN

Two Words on Design

The MIT Media Lab's **John Maeda** thinks simplicity is anything but easy to achieve.

If you turn on your TV today, you may see a commercial for Target in which the word "DESIGN," big and bold, flashes on a screen filled with oddly dressed people running around. "Is this a kind of madness?" you might ask yourself. But as the vibrant imagery on the TV settles in your mind, you are forced to conclude, "Ah, this is … *design*." If you are a trained technologist, you will quickly shake yourself out of your trance and contradict that notion. "No," you'll think. "Design is about efficiency, usability, and structural elegance." I have spent the majority of my adult life wondering about this fundamental question: what exactly *is* design? And I'm still asking.



Some languages have different words for the different ways we think about design. For instance, in Japanese there is the word *sekkei*, which connotes designing a mechanism, system, or technology with rationalized metrics for quality. *Dezain*, on the other hand, goes beyond an object's function to how it makes us feel. The former can be thought of as the kind of design taught at places like MIT; the latter as the kind of design taught at art school.

An object that has been *sekkei*-ed to be flawless from an engineering perspective can elicit an emotionally empty response. An inspiringly *dezain*-ed object may incite passion, but if it is not *sekkei*-ed to be reliable, it will inevitably disappoint. Both *sekkei* and *dezain* are prerequisites for creating an object, service, or experience that is desirable in the marketplace. This is especially true today, as more and more products feature ever more sophisticated technology. Marrying technology with feeling is the dream that design in the 21st century seeks to realize.

But if one thing quickly surfaces when it comes to technology, it's the feeling that it is getting much too complex for everyone. We seek simplicity today in our interactions with all forms of technology, but we end up reading long-winded manuals or just giving up. I researched the quest for simplicity in design and technology for my recent book and ended up discovering how complex a subject simplicity really is. Simplicity is about how we feel; complexity is about the possibilities that technology brings. In an age when it's possible to engineer and build absolutely anything, we have time and opportunity to focus on the feelings, and not just the possibilities, that technology now affords. TR

John Maeda is associate director of research at the MIT Media Lab and author of The Laws of Simplicity.

BIOTECHNOLOGY

Genomes for the Masses

The proliferation and plummeting cost of DNA sequencing heralds the year of the personal genome, says **George Weinstock.**

This year may be remembered as the year of the personal genome. Last month, two companies announced plans to decode the genomes of individual human beings. A company in Branford, CT, 454 Life Sciences, is sequencing the genome of James Watson, the codiscoverer of the structure of DNA and an eminent figure in the genomics field *(see "Sequencing in a Flash," p. 72)*. And Illumina, a DNA analysis company headquartered in San Diego, CA, is sequencing the genome of one of the Yoruba people participating in the international HapMap project, the first effort to probe the structure of diversity in the human genome on a large scale *(see "Genes, Medicine, and the New Race Debate," June 2003)*.

Whereas the DNA sequence produced by the Human Genome Project in 2003 was a mosaic drawn from a number of different human genomes, the efforts by 454 Life Sciences and Illumina, which could be completed in the next few months, will be the first sequences of individual genomes. As such, they herald the era of "personalized genomics." An individual genome sequence shows the particular combination of genetic variants in an individual's DNA, allowing scientists to explore the relationship between a person's genotype and his or her biological traits. This has been done at the level of single genes for decades, but never before on the genome-wide scale.

What has brought genetics to this point is the rapid development of new sequencing technologies over the last few years. Both Illumina and 454 are marketing DNA-sequencing instruments that depart in their chemistries and methods of detection from the traditional "Sanger sequencing" technology, which has dominated the field for the last 30 years. Following close behind Illumina and 454 are several other companies that expect to have new sequencing instruments on the market this year.

Much of this activity is driven by an $83 million investment by the

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ECONOMIC DEVELOPMENT ALLIANCE

NIH's National Human Genome Research Institute, which sponsors development of sequencing technologies to produce a $100,000 genome and eventually a $1,000 genome. These new technologies should deliver a human draft genome—meaning a sequence with gaps and some errors—for $100,000 by next year. Will this drop to $1,000 by 2013? I would not bet against it, given the progress since a few years ago, when the cost of a draft sequence was 150 times what it is now.

Some technical challenges still lie ahead. A draft sequence is assembled from millions of random, short component sequences; the longer the components, the easier the whole genome is to assemble, with fewer gaps in the finished product. In Sanger sequencing, the fragments are 800 bases long; with 454's technique, they are about 250 bases; and with Illumina's, they are 30 bases. This year we will begin to learn the utility of draft DNA sequences produced by the new technologies.

By the way, a $1,000 human sequence would mean that a bacterial sequence would cost around $1. The human body has more than 10 times as many bacterial cells colonizing it (the human microbiome) as human cells. And unlike the human cells, which are all pretty much the same, bacterial cells represent tens of thousands of species. So it is not surprising that NIH and other agencies worldwide are beginning to mobilize for a Human Microbiome Project. But that's a story for another time. TR

George M. Weinstock is codirector of the Human Genome Sequencing Center at Baylor College of Medicine in Houston, TX.

ENERGY

Global-Warming Myths

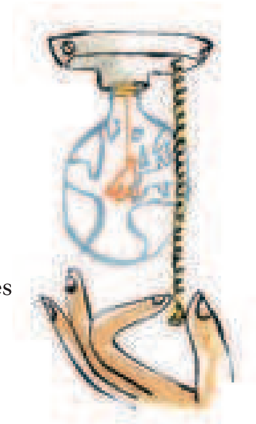
It's time to move forward on regulating greenhouse gases, says **Hoff Stauffer**, and here's a regulatory plan that makes sense.

The debate on global warming is burdened with unfortunate misconceptions that inhibit progress in moving forward *(see "Planning for a Climate-Changed World" p. 62).*

One misconception is that "draconian measures" would be required to mitigate global warming. This is simply not so, if we implement a prudent program right away. Such a program would include four major strategies: increased energy efficiency (in buildings, autos, and appliances), coal mitigation (which includes increased use of solar, wind, geothermal, and perhaps nuclear power, as well as carbon capture and sequestration for coal-fired power plants), the development of new biofuels (such as cellulosic ethanol), and reversal of deforestation. These strategies can stabilize atmospheric concentrations of greenhouse gases at acceptable levels and for acceptable economic costs.

Another misconception is that it would be better to wait to take action until technology provides new options. In fact, we need to start reducing emissions right away. If we delay, the world *will* face a dreadful dilemma: the choice between adopting draconian measures and passing the "tipping point beyond which it will be impossible to avoid climate change with far-ranging undesirable consequences," as the NASA climate scientist James Hansen puts it.

Another misconception is that a cap-and-trade system is the best approach to controlling the various greenhouse gases. Such a system sets a cap on total emissions and distributes emission allowances (or permits to emit) to market participants. These participants must buy allowances if they don't have enough, and they may sell them if they have an excess. Such a system has helped reduce sulfur and nitrogen emissions from power plants in the United States.



But there are major problems with relying too heavily on this approach. The biggest is that it is too hard to figure out the economic and environmental effects. Prudent people do not want to risk unacceptable economic consequences. Other prudent people do not want to risk accomplishing too little. A politically acceptable compromise might take a long time and would probably tilt too far toward economic prudence, failing to achieve the necessary reductions.

Performance standards are a simpler approach. They would directly regulate the pollutants from new sources of emissions, such as power plants and autos, and mandate greater efficiency for new appliances and buildings. Performance standards can be implemented right away, without fear of unforeseen adverse economic consequences. They alone would result in major emission reductions over time. Such reductions could then be complemented by whatever additional help a cap-and-trade system provides. TR

Hoff Stauffer is the managing director of the Wingaersheek Research Group, which focuses primarily on global climate change. He previously worked at the U.S. Environmental Protection Agency and various consulting firms.

Photo Essay

Objects of Desire

We asked prominent designers featured in this issue to help us see, through their eyes, pieces of technology that have influenced the way they think about their work.

By Katherine Bourzac Photographs by Bruce Peterson

1972, Polaroid SX-70

Polaroid's first fully automatic, motorized camera was an instant design classic, even starring in a documentary the year it was introduced by company cofounder Edwin Land. The camera is detailed with tan leather and folds into a rectangle the size of a paperback book. Andrew Logan, principal designer at Frog Design, admires it for the "immediacy of a favorable output." He explains: "Instead of waiting days to see if you took a good photo, you could take it again right away."

1977, Atari 2600

The Atari "almost predates the Mac in making computers friendly," says Mark Rolston, vice president of creative at Frog Design. "It was sitting on the floor, being used by 10-year-old kids. It's burned like a brand in the brains of people my age, because that was our childhood." Rolston's colleague Logan says, "Games were played either on big and bulky arcade machines or on a computer. The Atari did a great job of scaling. It sold at a price point average families could afford."

Photo Essay

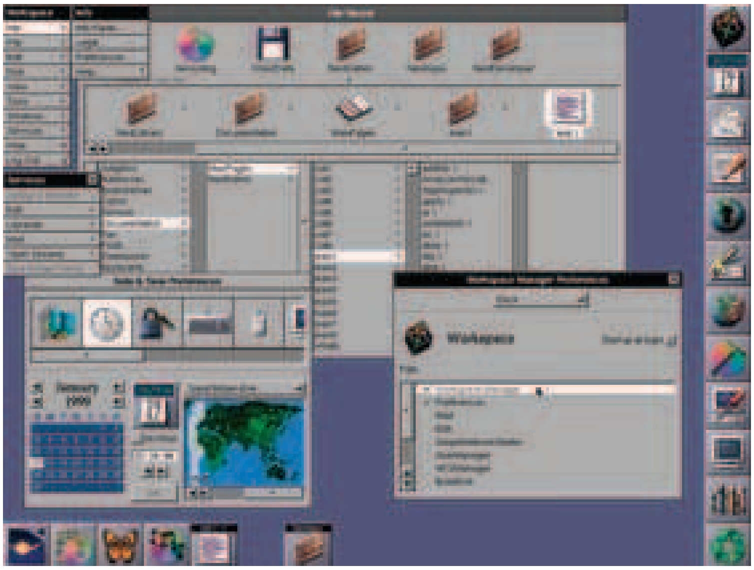
1979, Sony Walkman
"It has simplicity of use," says Logan. "You could give it to someone who's never used one before and they can use it. You can only get that with reduction of features." Though the early Walkman had two headphone jacks to let users share their audio experiences with friends, the device was a good way to annoy your parents by being present but absent, says Rolston. "The social phenomenon of people walking around immersed in their own private world was kicked off by the Walkman. I remember the response when you put on your headphones. Your parents would look at you like you killed someone."

1981, HP 12c Calculator
"It *is* the calculator. The way it looks is what you think of when you think of a calculator," says Rolston. Logan adds that it "took an existing technology and improved on it through design and manufacturing." This classic financial calculator uses reverse Polish notation, a system from the 1920s that, once learned, saves the user the trouble of using parentheses and brackets to write out mathematical expressions. Logan admires the 12c's staying power. "It has a great quality of build. It's still used by people. It's an example of how to build a product if you want it to stay around."

1983, Motorola DynaTAC 8000X

"Old things are precious, aren't they?" muses the MIT Media Lab's John Maeda. "First objects are always daring." The 8000X, the first commercially available cell phone, took Motorola more than a decade and $100 million to develop. Today, with the heft of a dumbbell, it is an object of nostalgia.

"I have a collection of old Motorola phones," says Maeda. "I like looking at these things. But I don't miss them, because they're large and clunky. You look at old TV shows and they pull out these shoe-size things. They make a better phone, because they're just phones. Now phones are GPS and Web enabled with a heart-monitoring system just in case. I keep old cell phones on my windowsill to look at. I should probably throw them away."



1988, NeXT OS
"In college I went out of my way to go to workstations with the NeXT OS. I was able to take mundane Unix tasks and do them with a good graphical user interface," says Matias Duarte, vice president of experience design at L.A. mobile-communications firm Helio. "That type of OS as a category is iconic, but the whole windowing and pointing paradigm is really old. I expected better by the 21st century. It's about time we started to break through the constraints of that paradigm." Shown here is a mid-1990s version of the NeXT OS, NeXTSTEP.

1994, Netscape
"If you look at a modern browser like Internet Explorer or Safari, you see the URL bar, the Back and Forward buttons, Home, and Refresh," says Rolston. "We've added things, we've made it prettier, but the browser hasn't been reinvented. The original Netscape design deserves the credit. Outside the browser and the shape of computers, this space [PC-era design] has yet to produce lasting icons in a grander sense, an iconic form that is reproduced over and over."

1995, Amazon
"Amazon is iconic, but not necessarily good design," says Rolston. "A Jeep is iconic, but if you've ever ridden in a Jeep, it's crap. Amazon represents a basic approach to e-commerce. It's balanced cacophony: there's search, reviews, and comments swirling around these pages. With these tools, you almost serendipitously end up with a basket of things to buy. It's iconic because it nailed early on the basic approach of a vast catalogue."

Photo Essay

Palm V
3Com
March 2007
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1999, Palm V
"If I had to pick one product as the best of the last 20 years, it would be the Palm V," says Duarte. "It has the three essential attributes of design: substance, style, and simplicity. It set the essential feature set for a PDA. Its metallic case had no exposed screws or fasteners. The hardware and software set were part of one experience. Its leather cover and metallic body really made it a fashionable accessory item you could create an emotional relationship with. Before the Palm V, you were happy if you could get a device with the right feature set. If it was always easy to use, you were ecstatic. Style was unusual. Once an object reaches technological maturity, it becomes about an aesthetic feature set. In the consumer electronics industry, we're constantly riding that wave."

2006, MacBook Pro 17"
Bill Moggridge, who designed the first laptop, the GRiD Compass, in 1979, calls this Mac "the nearest to the ultimate laptop that has been achieved to date, for its huge and delicious display as well as for its elegant and refined appearance and proportions."

Careers in Motion

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Career Growth Profile

ALEXANDER KHAW
Age: 25
Job Title: Associate of Manufacturing
Employer: Amgen Inc.
Program: MS, clinical lab sciences/ biotechnology, URI

A year and a half ago, Alex Khaw found himself in the right place at the right time. Almost immediately after throwing his cap in the air upon graduating from Northeastern University with a bachelor's degree in chemical engineering, he walked right into his first job. To his good fortune, Amgen, a Fortune 500 company that specializes in human therapeutics, was in the midst of a hiring push. The international biotechnology company tapped Khaw to come on board as an associate of manufacturing at its facility in West Greenwich, Rhode Island.

"I was lucky," Khaw admits. "It was hard for many of my fellow classmates to find jobs straight out of college."

Working for a science-driven, entrepreneurial enterprise proved exciting for the 25-year-old, but Khaw soon discovered that to stay competitive in such a cutting-edge field, he would have to continuously update and expand his skill set. Only a year out of college, he decided it was necessary to return to the classroom—this time at the nearby University of Rhode Island to pursue a master's degree in clinical lab sciences with a focus on biotechnology.

"With how well the biotech industry is currently doing, I wanted to take classes that would help me better develop in that field," Khaw says. "While a degree in chemical engineering allowed me to gain a wealth of knowledge in the subjects of physics, calculus, and chemistry, I wanted something to fill in the gaps where I lacked in the subject of biology. I felt that having a well-rounded background in both engineering and biology would best aid me in going into a more research-based field later in my career."

Khaw now balances his full-time job at Amgen with a weekly night class—a schedule that enables him to earn three credit-hours a semester. If all goes as planned, he should complete his master's degree in two and a half years. The best part is that Amgen will reimburse Khaw for his tuition and textbooks at the end of each semester if he earns a passing grade.

In addition to financial support from his employer, Khaw says his direct supervisor makes it "extremely easy" for him to balance work and school.

"When I initially asked him how he felt about me going back to class, he said he thought it was a great idea; he highly recommended it," Khaw says. "He also has been very flexible with my hours to allow for me to go to school."

Yet, even with a supportive employer, Khaw doesn't pretend that juggling work, school, and a social life is the easiest thing to do. Like any new endeavor, it requires some planning and focus. The young engineer works in rotating 12-hour shifts, which can be taxing in itself. He may work two days followed by two days off, and then work three nights followed by three nights off. The nature of his work schedule makes it easy to fit in his weekly evening class, but Khaw admits the drill can get tiring at times.

"Truthfully, I spend a lot of time sleeping to adjust from working nights and days, but I also find time to play sports and hang out with friends," he says. "During my undergrad years, I was a real procrastinator, leaving things to the last moment and cramming everything all at once. But believe it or not, working for a year and then going back to school has really changed my study habits.

To read more on how Khaw manages to balance his career and education, visit www.technologyreview.com/resources/career/

Do you have a career success story? Send a synopsis to career@technologyreview.com.

Ask the Expert

Susan Kryczka, Director of Distance Education, Boston University. Susan has over 27 years of experience in the distance education field.

Succeeding in an online learning environment requires fundamental computer skills and a little determination. This type of learning environment offers a new level of convenience for students, but it also requires planning and preparation up front. Students regularly submit assignments, including homework, projects, and papers, through the Web interface. Like traditional classroom students, online students must also meet deadlines, so the curriculum is not entirely open-ended.

For more of Susan's expert advice, please visit www.technologyreview.com/resources/career/

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By David Talbot
Portraits by Gregg Segal

Soul of a New Mobile Machine

From conception to buzz, from three-way spring to soft-touch paint: inside the design of a multimedia communications gadget.

The headquarters of the mobile-communications startup Helio look out over the hip Los Angeles district of Westwood. The streets are packed with teens and 20-somethings—whose business Helio covets. The company aspires to hook them on the ultimate multimedia device: something perfect for talking and messaging, gaming and Web searching, social networking and finding buddies via GPS. By the end of this quarter, Helio predicts, its year-old service, which leases space on the Sprint network, will have more than 100,000 subscribers. But the company—a joint venture between the Internet service provider EarthLink and the Korean wireless giant SK Telecom—has already burned through much of its $440 million in funding; according to a U.S. Securities and Exchange Commission filing, Helio lost $192 million last year. Now its hopes are pinned on its newest, most radical device, the fullest expression of its corporate ambitions: the Ocean.

The Ocean is hefty by today's sleek standards, pill-shaped in a market of rectangular things. The company's future will hinge on how much the intended audience appreciates those departures from conventional design. It will hinge on the layout of the device's QWERTY keyboard. It will hinge on the simplicity of the messaging and search interface (for instance, the way it allows users to start typing from idle mode). And it will hinge on—the hinges. The Ocean (which will sell for $295, plus a monthly fee of $65 to $135 for rich-media subscriptions and varying allotments of voice minutes) sports a pair of them; operated by a novel three-way spring, they enable a keyboard to slide out from one side of the device and a numerical keypad to slide out from another.

In short, the Ocean's design will make or break Helio. "Basically, to us, design is the product," says Sky Dayton, the 35-year-old CEO, with the Westwood skyline framed behind him on a clear blue March afternoon. Dayton founded EarthLink at 23 and became rich by making Internet access simple. "We get up every day thinking about this," he says. "If you go talk to the CEO or COO of one of the major carriers, I doubt you will hear much about the color of icons, the feel of the soft-touch paint. I can wax

SKY'S THE LIMIT: **Helio CEO Sky Dayton holds the object of his new obsession, the Ocean handset. "Basically, to us," he says, "design is the product."**

poetic about the spring-loaded action [of the sliders].” And he does: “We really thought about the movement and the sound it makes when it opens, the sound it makes when it closes. You see a mannerism when people open and close their Ocean. It’s like humming to yourself.”

The mobile-communications industry, Dayton says, has long been a “design desert” dominated by phone companies interested mainly in rounding up subscribers by the millions. But achieving great design is a growing fixation. Nokia, for example, recently hired the famed design firm Ideo—whose gadget credits include the first mass-market computer mouse, in 1981, and the Palm V PDA, in 1999—to help reinvent the gaming experience for a new line of smart phones *(see Q&A, p. 30)*. “A cell phone is becoming this incredibly powerful repository for multimedia experiences,” says Duane Bray, who heads the software experiences group at Ideo and has no connection to Helio or the Nokia project. “Design is just supercritical, because we have to understand how to sequence it—what things live together in a smart way. The Web 2.0 phenomena of social networking and sharing, converging on the cell phone—that is an interesting trajectory.” People want to use their cell phones for many things, he adds, yet “the device still has so many inherent flaws—small screen, awkward inputs.”

This is the story of how one small company wrestled with those flaws—and gave birth to a new machine.

Hinge

In some parts of the Helio offices, the floors are bare sealed concrete. One wall sports a pink mural featuring some of the company’s brand icons, especially the “Helions.” They look a bit like a pair of male and female bathroom-door symbols holding hands, and their heads consist of Helio’s stylized flame logo. Helions appear in the mural as part of a tableau that includes elements of anime cartoons and psychedelia. In a break room, a pair of plastic guitars for the game *Guitar Hero* await contestants. (“Do you play?” Dayton asks.) Three days before I arrived, the Ocean had had its trade-show debut. The staff was still basking in the enthusiasm it had sparked, including some reviews that likened it to Apple’s much-praised iPhone. (One even suggested that the Ocean might be an “iPhone spoiler.” The notion was speculative, since neither device is yet available.)

Before the Ocean was unveiled, Helio had already made its mark with a series of social-networking milestones: earlier devices had been the first equipped with GPS-enabled Google Maps, to direct you to the bar where your friends have gone, and the first to become mobile outposts of MySpace, the better to upload your drunken photos. The goal for the Ocean was to be the best at all these things and more—messaging, picture messaging, Web searching, gaming, telephony, point-and-shoot photography—without

SLIDE HERE: **The inclusion of a full horizontal QWERTY keyboard and a full vertical number pad (extended at right) made the Ocean somewhat plump. To make the 22-millimeter-thick handset seem slimmer, Helio girdled its midsection with a silver band just five millimeters across at its widest point.**

PHONE PHOTOGRAPHS BY TOBY PEDERSON

compromising on anything. Connecting to one's friends was the organizing principle.

But pursuing that goal produced what Matias Duarte, Helio's vice president for experience design, calls a "critical conflict of requirements." In particular, to be the best e-mailing, instant-messaging, and Web-searching device, the Ocean needed the roomiest possible horizontal version of the full QWERTY keyboard. But to be the best phone, it would require a vertical orientation. Reconciling these and other requirements would force an early decision on form. Clamshell? Swiveling mechanism? Slide-out keypad?

The first glint of an answer came, unsurprisingly, from Korea, where mobile communications are a cultural obsession. In Korea, people play mobile karaoke. Teens flock to sports arenas to watch other teens play in video-game contests. And today, a fair number of Korean electronics wunderkinds work at Helio. Dayton calls one of them "Joe Kool—with a K." Joe Kool is, in fact, Jungyong Lee. Lee, a senior product-planning manager, used to work at SK Telecom. (Some previous Helio models were built by SK Telecom's frequent manufacturing partner, Samsung.) While at SK, he conceived of something novel: a mobile communications device with two slide-out control panels. When the gadget was being used as a phone, a number keypad popped out of the bottom. When it was being used as a music player, you rotated it 90 degrees and slid out a small control panel with the familiar buttons—Play/Pause, Forward, Back, Stop. "Nowadays we converge the music device with the phone," Lee says in the Helio break room. "Many keys will be needed. But we need to make it simple. So we need to hide the keys."

Lee's innovation was what Dayton calls "the germ of the idea" for the Ocean's basic dual-slide form. But the horizontal slider had to be a full QWERTY keyboard—far larger than Lee's music controller—in order to make messaging and search satisfying experiences. Most mobile gadgets with QWERTY keyboards cram them into a square, with the space bar or Delete key stuck in an unfamiliar place. The large horizontal slider provided more real estate to work with. The Ocean's designers put the space bar—the most-used button—between the V and the B, so you can hit it with either thumb. The Enter and Delete keys are about where they are on a full-scale keyboard.

But the dual-slide format brought on another problem: no one wanted a device that was too thick. A number pad and a QWERTY keyboard would normally require two sets of springs and hinges—one for each slider. This would tend to fatten the gadget. What's more, Helio wanted the sliders to be rugged and to have a firm "feel," like the luxurious *thwunk* of a BMW's door. "We need to avoid those indeterminate states, when it can slide halfway out, and it is neither fish nor fowl," Duarte says. The Ocean needed a very special kind of mechanism: a single spring that could not only control hinging action from two directions but impart that hum-to-yourself satisfaction to the keyboard-sliding experience.

Designing the spring required the expertise of product-engineering specialists. Most cellular carriers will hire a manufacturing company—a general contractor, if you will—and accept its solution to a given mechanical problem. Helio had hired Pantech of Seoul, South Korea, to build the phone, but it also hired a small engineering company, Teus of Suwon, South Korea, specifically to solve the hinge problem. Teus's people came up with something new in the realm of mobile communications: an ingenious triangle-shaped spring that governs the opening and closing of both of the Ocean's sliders. The triangle simply gets pushed on different sides, depending on which slider is being used. Using one of the sliders feels like pushing something over a little incline and then dropping it firmly down into a locked position. With the design of the spring, Helio was on its way to a device that worked well as both a phone and a messaging device—without being too fat.

The Ocean needed special hinging mechanisms that could control two slide-out keyboards without making the gadget too thick. A Korean subcontractor solved the problem with a single triangle-shaped spring that governs both sliders.

D-Pad Dilemma

But while the hinge spring made the dual-slide concept feasible, the dual-slide concept brought on the d-pad problem. "D-pad" means direction pad: four arrow keys with a center button. For messaging and Web surfing, the d-pad should be to the right of the screen. This is because most people use their right thumb to navigate. But in gaming, the right thumb has a more important job: it must keep up a rapid staccato on a firing button. So for game consoles, the d-pad needs to be on the left. Another Korean engineer at Helios, gaming-product manager Leo Jun, insisted that if the Ocean was really going to be the best of everything,

there could be no compromise on the d-pad. The device had to have a left-side pad for gaming—whether or not it also had a right-side pad for messaging. It was another "conflict of requirements."

Jun's solution: give the device not two orientations but three. The first orientation, of course, is vertical—for the phone. The second, with the QWERTY keyboard open, is horizontal; in this configuration, the d-pad is on the right, for scrolling through messages. The Ocean's software changes the orientation of the displayed material depending on which slider is pulled out. But Jun asked game manufacturers to give Helio versions of their software that essentially played upside down. Flip the device 180 degrees, keeping both sliders closed, and the game is now playing right-side up—with the d-pad on the left. "That was a nice move on his part, so it doesn't undermine the gaming experience," says Duarte.

Now there was the problem of the "soft keys"—keys that do different things at different times, such as navigate options or open up an e-mail list. Most users expect these soft keys to be in the same basic place, relative to the screen, no matter what they're using the device for. "The mind builds up relational patterns," says Duarte. "You remember *the thing at the lower right of the thing I am looking at.* You associate this with function—to bring up your contact list, for example." But since the Ocean has different orientations, the user will anticipate soft keys in different places, depending on how the device is being used. So Helio gave the Ocean four soft keys, two on either side of the screen. The dual-slider problem begat the d-pad problem, which in turn led to radially symmetric soft keys.

Once the layout problems had been solved, size became a concern. Early in the design process, the Helio designers had settled on a pill shape: they thought it elegant, and they believed it would make the Ocean stand out in a market crowded with squares and rectangles. "The pill is beautiful, but hard to make," says Duarte. "Most [internal] components are rectangles, and the most efficient space for packing them is a larger rectangle. We had a lot of trouble [getting] manufacturers to do a pill, because it had never been done before." And the shape indeed created some problems.

The Helio designers had wanted to keep the device to about 100 millimeters long by 55 millimeters wide. But in fitting square objects into that area—chips, screens, batteries—they had to square off the round corners, losing the pure pill shape. Eventually, Helio mocked up an advanced version of this revised design—one of several that were made along the way. It had looked fine on paper, but when the prototype came back, everyone knew it was wrong. It just didn't have the strikingly different pill-shaped form. "It had all the negatives of a pill shape—we couldn't use the corners—and none of the positives," Duarte says. So the prototype was tossed out: "We had to redo all of the tools. Those were some painful times."

Plus, they had to "increase the LCD screen," as one of the product engineers, S. K. Kim, puts it. Why? "It was actually Sky," Kim says. The boss decided he wanted a bigger screen—2.4 inches instead of 2.2 inches long. Dayton's desires could not be engineered away. Nor could the growing demand for power. Generally, the Ocean's engineers minimized power consumption with software that put functions to sleep; some hardware choices, such as a separate microprocessor for playing music, helped too. But the device needed to endure a full multimedia workout all day—gaming, phoning, and messaging—before requiring a charge, so it was hard to get away with a small battery. All this drove the device toward somewhat larger dimensions: 115 millimeters long, 56 millimeters wide, and 21.9 millimeters thick, bucking the trend toward ever-slimmer devices.

The appearance of bulkiness was a concern to everyone on the team. There could be no sacrifice of function, and no putting the Ocean on a diet. So the engineers sat down to figure out how to make their slightly bloated electronic jackknife appear as thin as an iPod Nano. The Ocean could not be made thinner, but it could be made to *look* thinner. As the old carpenters' saying goes: "Paint makes it what it ain't." Shininess and hardness can make a device seem larger; Helio chose a soft-touch black paint, partly for its slimming effect and partly for its somewhat minimalist look and slightly rubbery feel.

To further the illusion of slimness, a thin silver band encircles the device, in the middle of the soft black bulk. The eye sees the silvery line; the brain perceives thinness.

"The pill is beautiful, but hard to make," says Matias Duarte. "Most components are rectangles, and the most efficient space for packing them is a larger rectangle. We had a lot of trouble getting manufacturers to do a pill, because it had never been done." And the shape indeed created problems.

DESIGN DUO: **Matias Duarte (left), Helio's vice president for experience design, wanted the Ocean to be simple to use. J. W. Kim (right), senior director of product management, needed it to perform as many functions as possible.**

DUAL-SLIDE INSPIRATION: **The Ocean's dual-slide design was inspired by a dual-sliding device conceived by Helio product-planning manager Jungyong Lee when he worked at SK Telecom in Korea. In Lee's Korean gadget, music-player controls popped from the side; in the Ocean, a full horizontal keyboard does the same.**

And as a final touch to make the exterior as sleek and unobtrusive as possible, the buttons were made to appear black when the device was off but to light up when it was on. On the verge of the gadget's debut in late March, the design team rushed out to make this last-minute change.

Modeless Search

In a mobile gadget, design is not simply a matter of physical form. The interface, too, should be simple. Helio's goal for the Ocean was to allow a user to grab the device in its idle mode and type a few letters of an address-book entry, a message to a friend, or a Web-search keyword. The high concept: all your e-mail accounts, instant-messaging accounts, text messages, and picture messages would be accessible through one integrated interface.

This required negotiations with the companies—Yahoo, AOL, Microsoft, Google—whose e-mail programs (including Hotmail, Gmail, and Outlook) the Ocean would adapt, so that users wouldn't have to close one program to open another. "This is an experience you can't even get on the desktop," brags Duarte. "We had to build it all from scratch and have intense negotiations with partners, because they are all closed platforms."

The Ocean's designers also sought the easiest possible way to let users reach other people or search the Web. Typing a few letters will bring up your list of contacts: hitting *P* takes you to "**P**aul Smith," "Joe **P**arker," and so forth. Nothing novel there. But then came an idea: why not make this work for search terms, too? If you keep typing until your string of letters no longer matches a name in your contact list, it becomes a search term. Type in "pizza," hit Enter, and unless you have a friend named Pizza, you are now searching for pizzerias without even opening a Web browser.

Wonhee Sull, Helio's mild-mannered president and chief operating officer and another veteran of SK Telecom, is very proud of this feature, called modeless search. "When mobile devices came to realization, [companies building them] used the PC as a platform reference," Sull says. "They just tried to shrink their version of a PC application and plug it into a mobile device. That didn't work. It is a small screen. We wanted to give them the answer they want right away, rather than routing them through the whole thing. We didn't take the PC as a reference point. We started with 'What do people want to do with a mobile device?'"

The Ocean still cannot be all things to all people. Like many other mobile devices that aren't iPods, it cannot play copy-protected music purchased through Apple's iTunes. But this wall is coming down. Apple and EMI Music recently reached an agreement to give iTunes customers the option of paying more for EMI songs that can be copied to other devices. Apple CEO Steve Jobs says this option will be available for half of all iTunes songs by year's end. These more expensive audio files could be loaded and played on the Ocean. Meanwhile, the Ocean supports over-the-air music downloads (sold by Helio Music) and can play music in all formats covered by Windows Media copyright protections and sideload them to a computer.

Retail Therapy

Finally, Helio embarked on a quest for the holy grail of high-end consumer marketing: to use the jargon of marketers, the company wants to design a unique retail experience—indeed, a lifestyle—around its gadgets. To do this, it hired a creative director, Joe Spencer, veteran of such projects as the aluminum skin of Disney's "Carousel of Progress" exhibit. Spencer designed the Helio flame icon, the Helions, and the concept behind the Helio retail stores—four of them so far, in San

Diego, Palo Alto, Santa Monica, and Denver, soon to be joined by a fifth in New York City's SoHo. At the Santa Monica store one Friday morning, animations designed by Spencer's creative team played across several screens. In one, Helions with butterfly wings flitted about on a sunflower field, symbolizing the "cross-pollinating of ideas on a network," he explained.

Besides four "pods" displaying Helio products, the store also features prints of images—like the voluptuous "Sugarluxe Girls" by artist Chandra Michaels—that users can upload as screen savers for $1.99. "One of the design tenets of what we are doing is that we are not a typical gigantic phone company that has no lifestyle attached to it," Spencer says. Users can even come and get their devices "spa treatments"—pressured-air cleanings, alcohol rubs—for free.

In the half-hour I was at the Santa Monica store, only one customer showed up. Granted, it was a Friday morning, and the store had just opened. And the Ocean is not out yet—it goes on sale this spring. Only then will Helio know whether the stores will be packed with early adopters, drawn in by design, who will become hooked on a machine that delivers. At first, perhaps, interface and functionality will matter more than silver stripes and the thwack of a keyboard. "When a product category emerges, early adopters look from a functional perspective," says Steve Walker, vice president and global head of marketing at Sony Ericsson. "But when the market matures—with later-adopting consumers, who have less functional demands—the importance of the aesthetic design becomes proportionally more important."

Helio is certainly aiming at that larger market; it wants to sell phones to more people than geeks, or even hipsters in SoHo and Santa Monica. Already, the device is being discussed in the same breath as the iPhone. But just how the Ocean, the iPhone, and other do-it-all devices will compete and coexist in different markets won't be clear until the competition, and the shakeout, begin this spring.

Meanwhile, there is no rest for Helio's designers. Back at headquarters, after our chat, Duarte grabbed a Red Bull out of the fridge in the break room. "One might imagine we're working on future products as we speak," he said with a grin. TR

David Talbot is TR*'s chief correspondent.*

IN THE DETAILS: **Clear plastic coats parts of the first iPod, an example of the "double-shot" manufacturing process.**

By Daniel Turner
Photographs by Peter Berlanger

The Design Issue

Different

Inside (sort of) Apple's industrial-design machine.

Apple, Inc. has made an art of not talking about its products. Fans, journalists, and rumormongers who love it or love to hate it have long had to practice a sort of Kremlinology to gather the merest hints as to what is coming next out of Cupertino.

A case in point is this story, which was to be about the iPhone—about how an innovative and gorgeous piece of technology was conceived, designed, and produced by the vaunted industrial-design team at Apple. Along the way, it would address the larger question of how one company can so consistently excel at making products that become icons, win design awards, and inspire customers.

But the *omerta* that prevails at Apple proved too strong. Company representatives declined to speak with me, and sources only tangentially engaged with the industrial-design process said that they could not talk either. When I asked Paul Kunkel, author of the 1997 book *AppleDesign*, for tips on obtaining interviews, he laughed and said, "Go sit outside the design-group offices with a pizza." What follows is as clear a picture of the Apple design process as we could get.

Designers tend to speak about the "genetic code" of products and companies. Pontiacs and BMWs, for example, can be recognized but also distinguished from each other by their split grilles. In some products, such distinctive characteristics serve mainly to aid brand recognition. But in complex objects such as computers, they can also signal operational familiarity: a customer who knows how to use product A will be able to use product B.

To whatever degree Apple can be said to make products with a distinctive genetic code, they can also be said to have inherited most of their traits from a single parent: founder Steve Jobs. Jobs left the company in 1985 and didn't return until 1997. Nonetheless, according to many who have worked at Apple, sometimes in close proximity to Jobs, it was largely he who established the company's emphasis on industrial design. Indeed, some would say that he made design a higher priority than technology.

Mark Rolston bears the title of senior vice president of creative at Frog Design, a product-design and strategic-branding firm that worked closely with Apple from 1982 to 1988. (Rolston did not work directly on any projects with Apple.) The company's projects have ranged widely: retail display systems for Victoria's Secret; websites for Microsoft, Dell, and Yahoo; webcams for Logitech. In publicity pictures, Rolston sports a T-shirt and an indie-rock mop of shaggy blond hair that bespeak his years in Austin, TX.

Even in the early 1980s, Rolston says, "Jobs wanted to elevate Apple by using design." Jobs, he says, not only cared personally about design but saw that it could be a way to differentiate his company's products from the PCs of the day, which often looked little evolved from hobbyist boxes. Ken Campbell, a codesigner of the Apple Lisa, was quoted in Kunkel's *AppleDesign* as saying that Jobs wanted Apple to be what Olivetti was in the 1970s: "an undisputed leader in industrial design."

Through much of 1982 and into early 1983, Jobs searched for a sympathetic design partner; he finally found one in

Apple's designs in the Apple II era moved computers out of labs and basements and into dens, living rooms, and bedrooms: places where people form emotional attachments to the things around them.

Hartmut Esslinger of Frog Design. Together, the two companies developed the "Snow White" design language that was meant to give Apple's products a coherent visual vocabulary, the appearance of being related.

That vocabulary featured, among other things, lines two millimeters wide and deep, spaced 10 millimeters apart, to suggest precision. (Some of the grooves were functional, acting as vents for airflow.) Case corners were rounded, but to differing degrees: if the curve at the back of a computer had a three-millimeter radius, the one at the front had a two-millimeter radius, reducing the machine's perceived size. In addition, the rounded corners and lines echoed distinctive features of the Mac user interface of the time: rounded screen corners and horizontal lines in the grab bars of windows.

Such precise design requirements simply couldn't be met by the manufacturing processes used to make most consumer objects—and certainly computers—at the time. Most manufacturers cheat when making plastic cases: they use molds with sloping sides called "drafts," which let parts pop out more easily and make for simpler, cheaper production.

Jobs and Frog Design wanted "zero-draft" molding, which yields perfectly perpendicular sides but costs more. No other computer manufacturer at the time was using zero-draft molding, which helped give Apple's products a distinctive look. Also, the more-precise manufacturing process meant that the cases of Apple computers could fit more tightly around the internal components, saving plastic, packaging material, and shipping costs.

Much of Frog Design's expertise at manipulating plastics came from its experience designing cases for home electronics, for clients such as Sony in Europe. "That was the first success with plastics in casing instead of wood," says Rolston, remembering the days when TVs were built into cabinets or encased in fake wood paneling. "That's what moved electronic products away from the role of furniture." And Apple's designs in the Apple II era of the late 1970s moved computers out of labs and basements and into dens, living rooms, and bedrooms: places where people form emotional attachments to the things around them.

The company still works closely with manufacturers, according to Rolston. "Apple takes an amazing interest in material selection and how things are manufactured," he says. "They continually ask what a manufacturer can do for them." Frog Design's experience with PC maker Packard Bell, he says, was much different, given the company's emphasis on economy: "We had to ask what the factory already did and how we could accommodate it. We found out that their case came together at the last moment, so we made that part of our design decision and focused on snap-on faceplates."

But Apple, Rolston says, "will change a whole factory's process." What's more, he adds, the company keeps its eyes open for new manufacturing possibilities, no matter how obscure. One example is the "double-shot" method of combining layers of different or different-colored materials. Apple "saw that a manufacturer had a special process for this on a small scale," Rolston says, and incorporated layered materials into its designs—for example, the clear plastic layered over colored materials in iPods and older iMacs. "[Apple] pushed them to do it on a much larger scale. Apple helped the manufacturers master the process and product."

Robert Brunner says his team pushed manufacturers in the same way during his tenure as Apple's director of industrial design from 1989 to early 1996 ("I just missed Steve Jobs's return," he says, but he notes that before he

DESIGN AS LEXICON:
The Apple IIc (left, and this page) helped establish the "Snow White" design language.

left, he hired Jonathan Ive, who has since become—next to Jobs—the person most identified with Apple's design primacy). "For example," he says, "if a power supply was too big for the form we wanted to use, we told a manufacturer, 'Let's figure out a way to use a new power supply.'"

Brunner, who will leave San Francisco design firm Pentagram this year to open a new design and marketing firm called Ammunition, is no design slouch himself. His work is included in the permanent collections of both MOMA and SFMOMA. In appearance, however, he is the antidesigner. "If Hollywood made a movie about Robert Brunner, the only man who could play him would be Steve McQueen," wrote Nate Voss, introducing a September 2006 episode of the popular Be a Design Group podcast. This is a man whose latest work is a grill that is expensive, beautiful, and carefully detailed—but still very much a device on which men cook meat.

SIMPLICITY ITSELF: **The Mac Mini is Apple's most basic offering.**

Brunner estimates that today Apple spends 15 to 20 percent of its industrial-design time on concept—far more than most other computer companies—and the rest on implementation. He says that Apple rides herd on manufacturers, sending design-team members to factories for weeks at a time to see what can be done and to push manufacturers to find new solutions. If the designers see a true innovation, they can integrate it into their designs and check the quality of execution at the point of manufacture.

"That's why it's perfect," says Brunner, "and the reason this is getting done is because Steve Jobs is saying, 'Do it.'"

"Pushing companies to innovate is a virtuous circle," says Rolston.

Declaring the importance of industrial design may have at first been a purely emotional decision for Jobs, or he may have had some sense of design's subconscious importance to customers. Either way, those interviewed for this article say the emphasis on design was there at Apple's inception, and it was there because of Jobs.

That emphasis did persist in Jobs's absence. But the company's design process was different, explains Don Norman, who was vice president of advanced technology at Apple from 1993 to 1998. Norman, who now teaches product design at Northwestern University's Institute for Design Engineering and Applications and serves as a principal at the Nielsen Norman Group, a consultancy that focuses on "the human-centered product development process," led Apple teams that developed new technologies and helped develop the company's process for product design.

"There were three evaluations required at the inception of a product idea: a marketing requirement document, an engineering requirement document, and a user-experience document," Norman recalls. Rolston elaborates: "Marketing is what people want; engineering is what we can do; user experience is 'Here's how people like to do things.'"

"These three [documents] would be reviewed by a committee of executives, and if approved, the design group would get a budget, and a team leader would be assigned," Norman says. At that point, he continues, "the team would work on expanding the three requirement documents, inserting plans on how they hoped to meet the marketing, engineering, and user-experience needs—figures for the release date, ad cycle, pricing details, and the like." And the team's progress would be continually reviewed as the project went forward.

It was a fairly typical process for the industry, says Brunner. "A division—portables, desktops, et cetera—would decide on a product they wanted to do and eventually engage the design group." Sometimes the design group would have early input on the product; but sometimes "we'd hear, 'You have two weeks,'" he says. "There was already a configuration set, and then it'd just be a styling task."

Norman describes Apple's design method back then as "a well-structured process" and says he is still proud of it. But he is quick to point out its shortcomings.

"It was a consultative process," he says; many different points of view and impressions were solicited. But "this can lead to a lack of cohesion in the product, when you find yourself asking another manager, 'What are you adding in?'" Rolston observes that within such a framework, "you'd get a cascade of people responsible for various factors injecting their concerns."

And, Norman adds, the consultative process could take a toll on the product line as a whole. Look, he says, at the 70-odd Performa models Apple churned out between 1992 and 1997—models that varied only in hard-drive size, in whether they had modems, or in whether they were sold directly or through a retailer.

"The businessman wants to create something for everyone, which leads to products that are middle of the road," says Brunner. "It becomes about consensus, and that's why you rarely see the spark of genius."

"Critical to Apple's success in design is the way Jobs brought focus and discipline to the product teams," Norman says. "[Jobs] had a single, cohesive image of the final product and would not allow any deviation, no matter how promising a new proposed feature appeared to be, no matter how much the team complained. Other companies are more democratic, listening to everyone's opinions, and the result is bloat and a lack of cohesion.

"The difference between BJ and AJ, Before and After Jobs, is not the process," he continues. "It is the person. Never before did Apple have such focus and dedication. Apple used to wobble, moving this way and that. No more."

One direct result of that sharpened focus is Apple's unique ability to create simple products. Though the idea of a simple high-tech device seems counterintuitive (why not offer more functionality if you can?), it's worked for Apple.

"The hardest part of design, especially consumer electronics," says Norman, "is keeping features out." Simplicity, he says, is in itself a product differentiator, and pursuing it can lead to innovation.

Rolston agrees. "The most fundamental thing about Apple that's interesting to me," he says, "is that they're just as smart about what they *don't* do. Great products can be made more beautiful by omitting things."

Brunner says that part of what makes minimalist design possible at Apple is the way Jobs structured the design group—and the way he privileged it. "The design leader has to walk a fine line," he says. "He has to be integrated with the company but keep his team members protected from being lobbied by marketing, engineers, manufacturers. They all have viewpoints on design." In recognition of these pressures, Apple has always kept its design team small—somewhere between 12 and 20 people, Brunner estimates.

"They're a small team that takes a very, very hands-on approach," adds Rolston. "We do a lot of similar products for other companies—say, Sony. But the process of approval, and collaboration generally—for everything from shape to engineering—involves tons of people, taking up to 50 percent of the time, watering it down." What makes Apple Apple and not Sony, says Rolston, is clarity of voice and vision.

And the secret to that clarity may be, like Edgar Allen Poe's purloined letter, hidden in plain sight. Sources will say, off the record, that Apple's design mavens shun interviews in order to sustain the idea that their success is the result of having a great team in place. But it may ultimately boil down to who hired and gave power to that team—Steve Jobs as not just an enabler but an active participant.

"Jobs is a dictator, but with good taste," says Norman. "He is good and driven to the perfect experience. He doesn't want good design; he wants great design." Brunner similarly lauds Jobs's "driven, singular focus." And Rolston says, in what is perhaps the best explanation of Apple's design ascendancy, "It's a happy coincidence at Apple that the designer in chief is the CEO. He has a fantastic sense of what people want. And after all, that is design." TR

Dan Turner is a freelance writer based in San Francisco. His work has appeared in I.D., Salon, *the* New York Times, *and elsewhere.*

Why Design?

Apple's designs are now the stuff of legend—and the object of fascination and envy. But is the focus on design worth it? Why spend time and money making a computer look good? Why do we care what it looks like?

"Attractive things work better," says Don Norman, who was vice president of advanced technology at Apple from 1993 to 1998. "When you wash and wax a car, it drives better, doesn't it? Or at least feels like it does."

Norman cites research in cognitive science suggesting that people's emotions affect the way their minds process information. In his 2004 book *Emotional Design*, he writes, "Positive emotions are critical to learning, curiosity, and creative thought. … The psychologist Alice Isen and her colleagues have shown that being happy broadens the thought processes and facilitates creative thinking."

In multiple studies, Isen, a professor of psychology and S. C. Johnson Professor of Marketing at Cornell University, made subjects feel happy through a number of means, including gifts of candy and words or pictures with pleasant associations. The subjects were then asked to perform tasks that measure creativity; over the course of 20 years, Isen and her colleagues regularly found that subjects exhibited much more creativity when they were in a good mood.

And conversely, Norman says, when you're in a bad mood, when you're tense, you tend to be less creative—and less patient with the tools you're using. "Someone in a positive mood," Norman says, "faced with something that doesn't work, might say, 'Oh, I'll get around it.' But someone in a negative mood will get frustrated and have a 'Damn it' moment." That's where design comes in. "Studies tie attractive design to positive attitude," he says.

By Roger Black
Portrait by Nathaniel Welch

Help Me Redesign the Web

The first epoch of Web design is over; from now on, Web pages will be as attractive as print—but more interactive.

The Web was conceived as a way for researchers and scientists to share documents, not as a medium for visual expression.

The aesthetics of Web pages, such as they were, derived from computer screens and typewritten documents. Early Web users no more felt the graphical limitations of the hypertext markup language (HTML) than they had resented having only one golf-ball font on their old IBM Selectrics. They were so delighted with the Net that the look was irrelevant.

First functionality, then bandwidth, and finally search were the key characteristics of good websites. Because people used a variety of browsers and operating systems to explore the Web, pages had to be flexible. The width of the window, the type size, the fonts themselves—all could vary and often did. The Web was so new and interesting, no one cared if it was ugly.

For many publishers and designers, New Media was born when John Gage, the Sun Microsystems evangelist, showed off the Mosaic browser (which later became Netscape) at the Seybold Seminar in Boston in April 1995. But some of the designers in the room stared at the big screen with little enthusiasm. To them, the browser was software, and that reminded them of work, but not of *their* work. Their control of the details, the high resolution of the printed page, the saturated color of photographs, the great library of typefaces—all this was threatened by New Media.

Like singing a song or writing a story, designing a printed page is a craft that is fundamentally unidirectional, or *one-to-many*. The flexibility of Web structures confounded and then humbled many traditional designers as they started trying to make Web pages. The whole thing had been developed to let the readers—the *users*, software developers confusingly called them, as if they were addicts—have control. How could that be good?

For these reasons, and others, most magazines' websites until very recently were dull, repurposed versions of their print editions. Thus, a new crowd took on the design of websites. These enthusiasts assumed that the print crowd *didn't get it*, that what they saw as the "new paradigm" would last forever. The two-way flow of information, the Web's flexibility, immediacy, and cheapness, deeply appealed to them.

But it was not as if these early Web designers were starting with a blank page. They had to work within the limitations of the graphical browser, which at first could not even be divided into frames. The Mosaic browser itself had to work within the clunky graphical-user-interface conventions of the Windows operating system.

Enter the Information Architect

By 1995, however, a generation had grown up with the personal computer. Adapting to the quirks of another Windows application was no big deal. A new kind of specialist, the information architect, emerged. IAs tried to create an overall logic for the design of a site. But as the Web grew, the IA guys formed a kind of priesthood, with its own mysteries. Some proceeded as if information architecture should be separate from design.

By 1999, with the dot-com boom in full roar, Web development teams had broken into mutually uncomprehending groups: software developers, information architects, search experts, and even usability experts.

Amid the pandemonium, a lot of people got rich, and understandably, they got a little cocky. The "netizens" and "digerati" dismissed the old print guys as wood-pulp fetishists, deservedly headed for oblivion.

The Web grew, and users got used to the conventions of the Web interface. But for all its powers, the browser is trapped in a world of pull-down menus and dialogue boxes. This is not an easy world to move around in. Because the Web is based on HTML, we should have guessed that users would end up moving from link to link. Google understood this. Search became the preferred way to move around because the Web had gotten so big and sites so confusing that the easiest thing to do was to enter a keyword.

At the very instant that search seemed dominant, the nature of the Web began to change. While it has always

As bandwidth increased, ads began to pulse and jive with Flash.

Today, every design student and professional photographer seems to have a personal site done in Flash—some with unworkable interfaces, some with weird drippy graphics, a handful with marvelously smooth and elegant screens that use striking typography and motion.

It's now possible to download whole Flash and WPF sites and run them when you want. One example is the *New York Times* Reader, for which I did some sketches, and which was reviewed on TechnologyReview.com *(see "The* Times *Emulates Print on the Web," May 2, 2006).*

The typefaces are the *Times'* own, and the fonts are clear. Columns are justified, and an algorithm limits the number of loose lines. If you resize the windows, columns reflow, pictures change size, and ads drop in and out.

Alas, Web designers are resisting new ideas like the *Times* Reader. But Web designers rejected Flash in the beginning, too. Perhaps it's unsettling for the digerati to realize that their new paradigm is *already* getting old.

For the rest of us, the possibility

been relatively easy to put stuff on a site, it became much easier with tools like Blogger and Movable Type, and simple blogs proliferated. With Friendster, and then MySpace, Web pages no longer came just from corporations, universities, and government; they came from everywhere.

But democratization did little to improve design. WordPress offered people templates for designed Web pages, but few bothered to modify them. Most blogs looked like blandly conventional websites. Although some creative folks put richer stories and picture scrapbooks on sites like LiveJournal, millions more just grabbed Web cameras and posted their videos to YouTube.

Going Beyond HTML

Design professionals, meanwhile, were turning away from HTML and moving toward the multimedia authoring technologies Adobe Flash and WPF (Windows Presentation Foundation, a competing technology from Microsoft). Advertisers, never satisfied with the look of the Web, started designing their ads as separate images, so they could control picture placement and use their own fonts.

of richer forms for Internet media is welcome. Communications will continue on the HTML Web, but now more-compelling storytelling in text and motion pictures is being brought online by new "clients" like Flash and WPF.

This may still not feel like home for old print designers who like to do things one page at a time, like artists. But TV, magazines, and newspapers are converging online and will soon enough appear on portable, cheap screens, carrying the branding of the old world, like the *Times* Reader. It won't be the old experience, though; it will have to be interactive.

Designers won't have much success in this new world if they try to design each rich screen one at a time. Already, the best Web designers make templates that work together in a design system. Why not make it possible for the users to adapt these as they see fit?

Maybe the way for designers to take control of the medium is to let it go. They should just design templates for everyone to use.

*Roger Black has designed more magazines than any other living graphic designer—*Technology Review *among them. He has also designed many websites, including Bloomberg.com and MSNBC.com.*


SLOW!
03

Planning for a Climate-Changed World

As the global picture grows grimmer, states and cities are searching for the fine-scale predictions they need to prepare for emergencies—and to keep the faucets running.

By David Talbot

On December 11, 1992, a powerful northeaster coalesced off the eastern seaboard of the United States, and an eight-foot storm surge struck New York City. Seawater swamped the Brooklyn Battery Tunnel to a depth of six feet, cascaded down PATH subway stairs in Hoboken, NJ, and forced LaGuardia Airport and many roads and subways lines to close. Had the storm been slightly stronger, a 10-foot surge could have devastated a far wider region, inundating low-lying areas like Coney Island and Manhattan's financial district and overwhelming the 14 sewage plants dotting the New York City coastline.

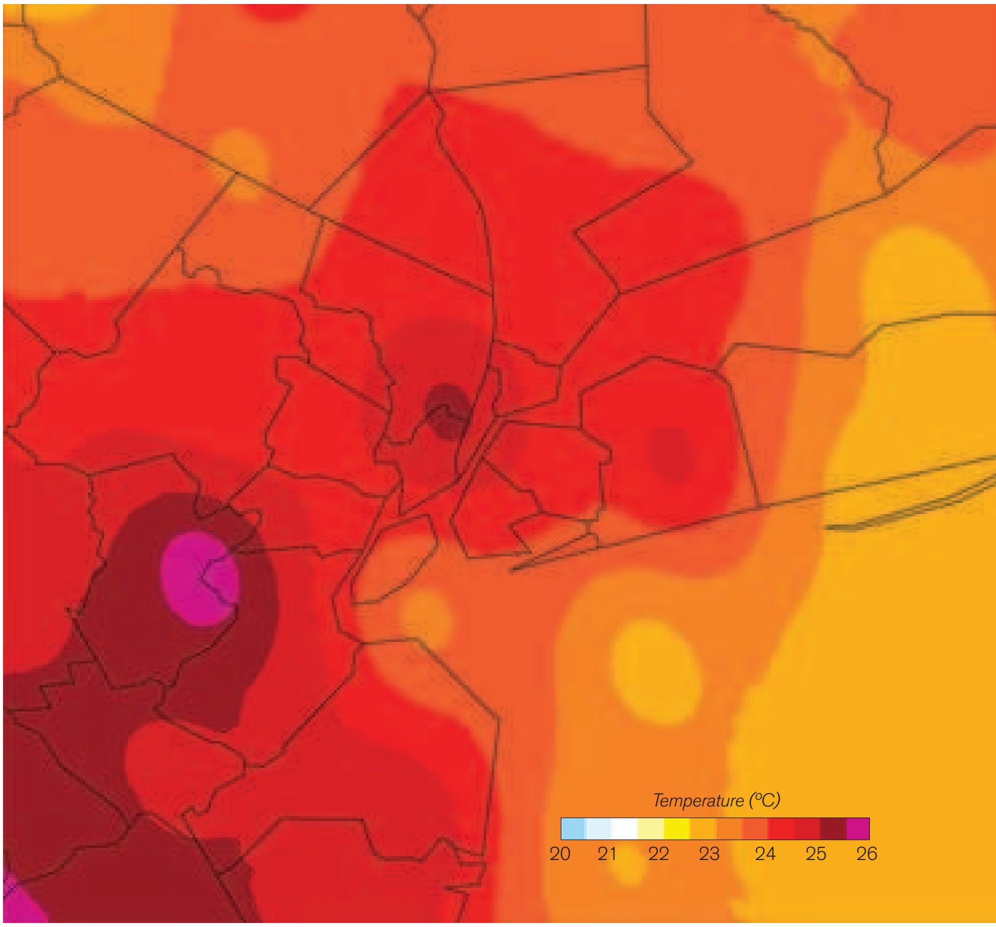
A flood of comparable height in New York City's environs should occur about once every 100 years, on average, in the estimation of one Columbia University study. But global warming and rising sea levels—as well as the possibility of more-intense precipitation, stronger storms, and altered storm trajectories—will make such disasters more frequent. And to protect the people who live and work where disaster threatens, the critical first step is to determine how quickly and by how much, exactly, the threat is increasing. That knowledge is essential to deciding how seriously to consider specific countermeasures; for New York, these could range from mandatory evacuation plans for seaside neighborhoods to multibillion-dollar storm-surge barriers spanning the Verrazano Narrows and other key channels.

But there are no clear answers, and part of the problem is that well-documented predictions about planetary change haven't generally been broken down in local terms. Though the Intergovernmental Panel on Climate Change (IPCC) has concluded with 90 percent certainty that human activity is warming the planet—and spelled out the likelihood of consequences that include higher seas, droughts, and fiercer storms—the United States is committing scant resources to providing usable information to the people who respond to emergencies, plan for urban development, manage coastal areas, and make sure the crops keep growing and the reservoirs stay full. "The challenge is to increase our capability to accurately forecast climate at the regional level," says Ronald Prinn, an atmospheric scientist who directs the Center for Global Change Science at MIT. "That is what is needed in order to improve the information that government agencies get—[and] to then translate those regional forecasts into something useful at the city [or] state level." Equipping people to deal with climate change could mean simply giving state and local planners access to a wealth of existing information—such as calculations made by the National Oceanic and Atmospheric Administration (NOAA) that could indicate how far inland storm surges would move if sea levels were higher. But it will also mean sharpening local and regional models, so that they can predict the effects of climate change in far greater geographic detail. And it will require new approaches to emergency planning, water-supply management, and more.

Global warming will affect different regions in different ways. In 2000, a national assessment by the U.S. Global Change Research Program (USGCRP) warned generally about potential climatic changes in what it called "mega-regions" of the nation. "What we were able to do at that point was very limited," recalls Michael MacCracken, an atmospheric physicist, now retired, who coördinated the assessment effort. And the study's climate scenarios were

DEREK BACON

based only on global models: "We really wanted to have more models, and more regional results, but we had very little resources to get that done." Similar, very general statements about climate change across large regions appeared in the most recent IPCC assessment, the first time the IPCC has narrowed its focus even that much. The report pointed out, for example, that the southwestern United States will probably get even more parched than it is now. But what we need are projections on a far finer scale. With federal climate-science budgets cut to the bone in recent years, a few state and local governments are funding their own efforts in New York, California, and western states eyeing dwindling water supplies with alarm.



Hot in New York, Hotter in Jersey

Global warming is an abstraction; people want to know how warm their own cities or counties will get. That's key to everything from agriculture to emergency planning. Global models typically provide estimates at a resolution of 150 kilometers. A regional model run inside a global one, however, can account for local topographical effects. The image above was produced by one such model: it shows average summertime surface temperatures in the 2050s, across counties in the New York metropolitan area. Knowing that it might be hotter in Manhattan than in the outer boroughs, and hotter still in parts of New Jersey, is vital for estimating, for example, the scale of health crises brought on by heat waves and ozone.

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A Wet New York City

Rushing into her office near Columbia University, Cynthia Rosenzweig was chipper despite her evident exhaustion. An agronomist by training, she directs the Climate Impacts Group at NASA's Goddard Institute for Space Studies (GISS) and advises New York City's government on how climate change will intensify heat waves, stress upstate watersheds, and increase the risk of a devastating storm surge. She had just returned from Delhi, India, where she cowrote a summary of the 2007 IPCC reports, the first of which was released in February. Brightly painted papier-mâché elephants she'd brought back from her trip were arranged on the coffee table in her sixth-floor office overlooking 112th Street (as it happens, some of the highest ground in Manhattan). She sat down and, on her computer screen, called up images from a GISS global climate model.

Honed by a broad range of climate scientists, the model represents atmospheric and oceanic systems. Like other global models, it simulates interrelated processes: for example, the warming of Earth's surface by solar radiation; the absorption of heat by the oceans; the reflection of solar energy by land surfaces, ice sheets, and particulates in the atmosphere; and the effects of the accumulation of excess carbon dioxide and other atmospheric gases that trap heat. Researchers test the accuracy of such models by seeding them with, for example, data on actual greenhouse-gas emissions over the past 30 years and then seeing whether they return results consistent with temperature and other measurements recorded over that period. The goal, of course, is a model that can predict how much temperatures will continue to rise given various future greenhouse-gas emission levels, and how other parts of the climate system are likely to respond.

But the limitations of global models quickly become clear when Rosenzweig zooms in on a map of the eastern United States showing climate predictions for the 2050s. On the screen, a line cuts from eastern Pennsylvania to western Massachusetts. The area north of the line is yellow, representing a 2 °C increase over historical averages; the area south of

the line is more orange, indicating a 2.25 °C increase. The entire New York metropolitan area, Connecticut, and much of Massachusetts and New Jersey are lumped together under a single temperature estimate. The same goes for several other variables, such as precipitation and evaporation rate. The problem is that one "grid box" in the typical global climate model—think of it as a pixel in a photograph—is a square of 150 to 200 kilometers per side.

Weather and climate are, obviously, far more localized than that. Mountain ranges—even individual peaks and valleys—make their own weather. A single glacier might grow or dissolve because of temperature and rainfall changes in a very specific area. Differences in air temperature over water and land cause breezes that can dramatically influence climate and weather in coastal areas. Regional models that take such phenomena into account are familiar to any viewer of TV weather news. But where global models are calibrated against data spanning decades, regional models are used to project only a few days ahead. Thus, one goal of climate scientists is to find a way for the twain to meet, to give local precision to predictions about global warming and climate change.

Rosenzweig's group has calculated that today's one-in-100-years New York flood would, in the 2080s, be considered a one-in-40-years or perhaps a one-in-four-years event. The order-of-magnitude difference is simply the result of variations between models. To calculate a more useful range of probabilities, Rosenzweig is currently combining global models with regional ones. By "nesting" models of smaller regional areas in the global grid boxes, she hopes to increase the resolution of climate-change predictions to 10 to 15 kilometers. In six-hour time increments, a global model introduces a fresh batch of climate variables into the regional models, which then make local calculations.

The project is ongoing; so far, efforts to validate such nested regional models against actual temperature measurements have shown the predictions to be off by 1 °C or more, an unacceptable margin of error. Still, Rosenzweig expects that regional models will become more precise with further work. And as they do, one of their uses will be to better predict storm surges by accounting for changes in local wind patterns. "The large majority of climate impact studies have been done with the GCMs," Rosenzweig says, referring to global climate models. "We are just now beginning to do more with the RCMs [regional climate models], and they are very much in research mode. Sea-level rise is the number one vulnerability, and we need better information for the agencies. It's critical for their planning."

To be sure, global sea-level projections are still a matter of debate: the IPCC pegged the 21st-century increase at between 18 and 38 centimeters under a scenario that assumed lower greenhouse-gas emissions and between 26 and 59 centimeters with higher emissions. This uncertainty makes perfect storm-surge predictions impossible. But the lack of information about local climate change remains a stumbling block that prevents New York City—and every other coastal area—from developing the detailed information it can act on. "You don't always protect against the worst case, because you would bankrupt the city," says Rohit Aggarwala, director of long-term planning and sustainability under New York's mayor, Michael Bloomberg. "How urgent is it to invest in multibillion-dollar projects? Knowing that over the whole Atlantic seaboard there will be *x* sea-level change and *x* change in violent storms doesn't necessarily help New York City make different decisions than Miami or Halifax." On the other hand, he notes, if New York were to operate on incorrectly optimistic information and delay the most ambitious storm-surge barriers too long, the consequences could be disastrous.

New York City authorities have already gotten some specific warnings from Rosenzweig's group, which made a study of how the city's water-supply and sewage-treatment infrastructure could be affected by rising sea levels. For example, a pump station north of the city on the Hudson River—built to draw emergency fresh water during times of drought—will eventually require expensive new filtration systems as rising seas push salinated water to within range of the intake areas.

But while there's still uncertainty about the rate at which sea levels are rising, it has become increasingly clear that temperature increases alone could severely tax a large city's infrastructure. Late last year, the Union of Concerned Scientists in Cambridge, MA, released a report titled "Climate Change in the U.S. Northeast." Produced in collaboration with climate scientists, the report predicts that by midcentury, northeastern cities could be experiencing an average of 30 to 60 days of temperatures above 90 °F each year, up from 10 to 15 days historically. By the end of the century, these cities could see 14 to 28 days of temperatures over 100 °F, if the higher-emission scenarios are realized.

Armed with such predictions, the city of New York and a prominent regional civic-planning group, the Regional Plan Association (RPA), are starting to think about how to respond. Jennifer Cox, a senior planner and director of geographical information systems at the RPA, is superimposing estimates of heat waves and storm surges onto city maps showing topography and socioeconomic characteristics. And GISS is collaborating with a consortium of universities whose members are now plugging temperature estimates into air-quality models, to see how bad ozone levels could get during the hotter summer days of the 2040s or 2060s. High ozone levels could produce severe health crises as heat waves overwhelm emergency facilities, water supplies, and the power grid.

But such studies are just the first academic pass at planning. The scenarios they envision are still relatively vague. And while suggested remedies abound, they reflect more imagination than engineering. Physical oceanographer Malcolm Bowman of the State University of New York at Stony Brook, for one, would place a tidal-surge barrier at the Verrazano Narrows (between Brooklyn and Staten Island); another near the Throgs Neck Bridge, where the East River meets Long Island Sound; another between Perth Amboy, NJ, and Staten Island; and a fourth across Rockaway Inlet at the entrance to Jamaica Bay. The barriers—more ambitious versions of the storm-surge barrier at the mouth of the Thames River outside London—could theoretically prevent tens of billions of dollars in damage. With the models and computational power available now, however, it's hard to determine whether and when such ideas need to be acted on. "If you look at European experience," says Bowman, "it takes a major flood and a major loss of life to get the bureaucracy to do anything."

The Dry West

Colorado Springs, CO, is a boomtown in an arid region—just one of many cities that rely for water on the melting snowpack of the nearby mountains, delivered via the Colorado River and Arkansas River watersheds. Many other cities get their water similarly from the Sierra Nevada Mountains of California. But right now, the western United States is facing a slow-motion water-supply catastrophe wrought by climate changes that will inexorably reduce the snowpack. "The western U.S. is really not in good shape at this point," says Linda Mearns, a climatologist at the National Center for Atmospheric Research (NCAR) in Boulder, CO, where she is director of the Institute for the Study of Society and Environment. This has become fairly clear "even without the regional detail" in climate models, she adds.

But the regional detail is still important for deciding how, where, and when to respond. Consider the Homestake Reservoir. High in the Rocky Mountains, not far from Vail, CO, it is part of a network of reservoirs and pipelines that feed water to Colorado Springs. In June 2006, the reservoir filled at the unprecedented average rate of nearly two feet per day. Because of higher temperatures earlier in the season, the snowpack was melting more quickly than usual.

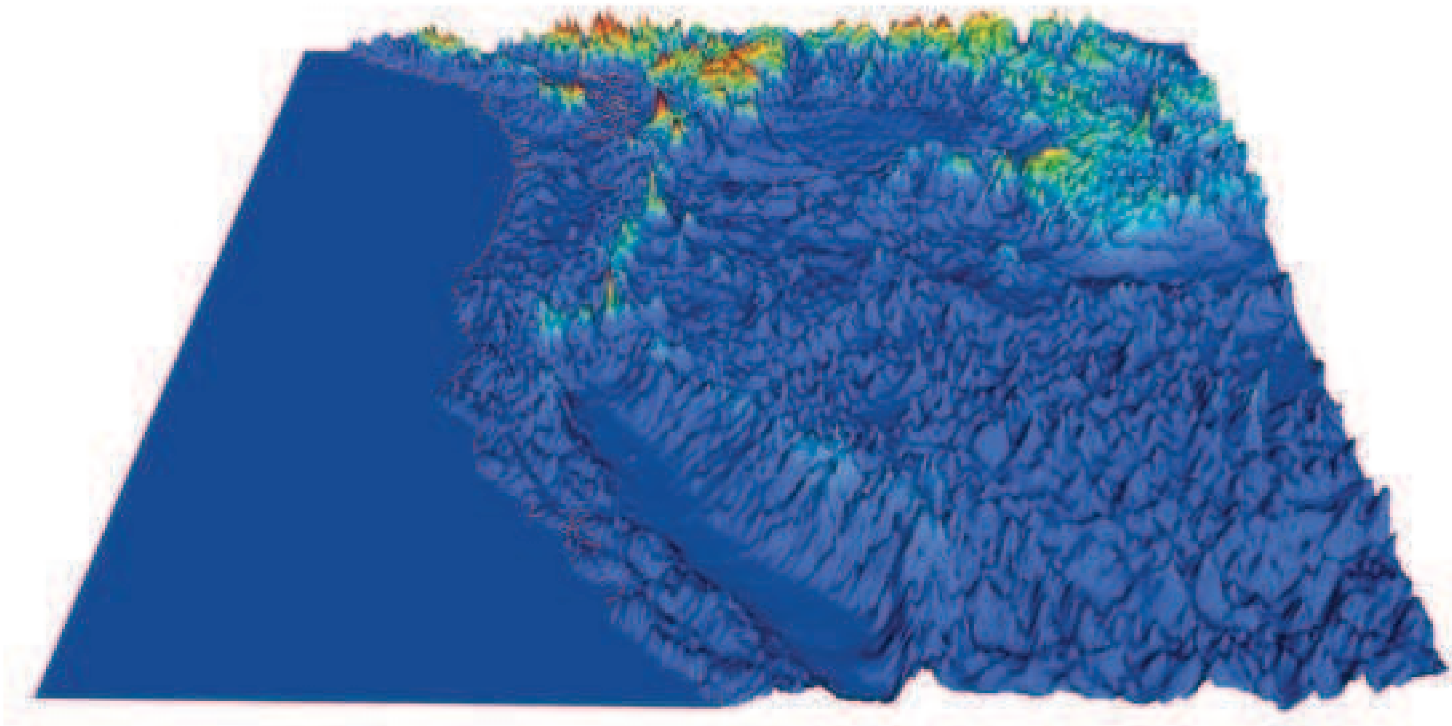
The unprecedented may become routine as global warming makes more precipitation fall as rain, while what snow there is melts ever faster. That's worrisome: a reservoir that fills more quickly than expected can stress a dry levee. And there are other concerns. At what point will earlier snowmelt translate into summer water shortages? Will early spring torrents raise the risk of downstream flooding? Will more-intense spring rainfalls increase sediment, overwhelming filtration systems and washing more pollutants into the water supply? And these climate-related questions arise at a time when rapid population growth is already stressing water resources.

Planners need to understand as precisely as possible the amount, timing, and form—rain or snow—of future precipitation. Only then can they determine when and where to build new water-storage, flood-control, and filtration systems and how to guide future residential or commercial development in watershed areas. So last winter, in a windowless conference room in an industrial area of Colorado Springs, engineers from Colorado Springs Utilities met with David Yates, an NCAR hydrologist, to start revising their water-supply management plans in light of climate-change projections. "Plans are typically made based on historical 20- to 40-year stream-flow averages," Yates said. "That mode of planning is no longer relevant."

Concrete local projections are especially important in this region, where politics constrain the way scientific findings can be discussed. Colorado Springs is a politically conservative city and home to a powerful Christian evangelical organization that is skeptical of concerns about global warming. Toward the end of the meeting, the utilities' manager of water-supply resources, Wayne Vanderschuere, entered the room. He was already thinking about how any new climate-change-related findings might be framed. "All the talk about climate change and CO_2—we don't want to go there. We don't want to talk about Kyoto, all the posturing," he said, referring to the Kyoto Protocol, the U.S.-rejected treaty that mandates limits on greenhouse-gas emissions. "We just want the analytic risk to supplying water that this poses."

Brett Gracely, the utilities' planning supervisor, said Colorado Springs was at a turning point. "We're trying to get a handle on what this all means for us," he said. He—and his city, and the rest of the country—just aren't sure exactly when and to what extent global trends will influence regional trends and make existing hydrology models obsolete. "If it comes down to literally building a model, how do we do that?" Yates asked during the meeting. "What needs to be done—what resources are needed to do that?" Colorado Springs' effort to build a model of how climate will affect local hydrology has just begun and could take two years.

One strategy the model is likely to use is to break down mountainous regions into elevation bands rather than small, uniform grid boxes. Mountain areas, with their myriad microclimates, are particularly difficult to model. Mountains can cause winds to shift and clouds to form; snow-covered north faces, warm south faces, and cold valleys can give rise to strikingly different conditions. L. Ruby Leung and Steve Ghan, climate physicists at the Pacific Northwest National Laboratory in Richland, WA, are pioneers in the elevation-band approach, which they say can be as accurate as nesting



Visualizing Water Shortages

Critical to understanding future water shortages in the western United States, the model that generated this image depicts springtime snowpack at a resolution of 1 kilometer, far better than the 150-kilometer resolution of the average global climate model. Red peaks indicate the deepest snowpack; purple areas indicate none. (The vertical scale is exaggerated; California's central valley is in the foreground.) This visualization incorporates data on clouds, surface temperatures, and precipitation, broken down by topographical elevation in a technology pioneered at Pacific Northwest National Laboratory. Zooming in on different regions reveals future snowpack loss on specific mountains ***(see "Vanishing Yosemite Snowpack," p. 70)*****.**

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techniques that zoom into smaller regions to resolve mountain effects, yet less computationally expensive. Their models provide, among other things, detailed pictures of how global warming will cause snow lines to move to higher altitudes, making it possible to estimate the resulting diminution of the snowpack that now provides most of the fresh water in the western United States. The state of California has already estimated that under scenarios assuming medium to high levels of future greenhouse-gas emissions, higher temperatures could eat away between 70 percent and 80 percent of the Sierra snowpack by century's end.

But so far, the models Leung and her colleagues have developed are not reliable enough to dictate specific measures for addressing snowpack loss—like building new reservoirs. Water-resource managers want more certainty, Leung says, so she is pushing the research on several fronts by running multiple global and regional models. Such efforts are both labor and computation intensive, but they are also critical to reducing uncertainty. "We know that the climate is actually changing, but they are managing the water system based on rules devised 50 to 100 years ago," Leung says. "If what we project in the future is correct, we expect a pretty big problem."

The Canaries

The rich can buy state-of-the-art climate science, just as they can buy state-of-the-art health care. And upstream from Colorado Springs, the resort town of Aspen, CO, kicked off its very own climate-change impact study two years ago. City leaders called it the Canary Initiative—because in their view, mountain areas could be the climate-change equivalent of the canary in the coal mine. They sought out the advice of leading lights in climate science and devoted a modest $145,000 to a pair of local studies. The announcement of the studies' findings last year bore the somber headline "Aspen Climate Study Finds Serious Risk to the Future of Skiing."

At first blush, the emphasis on skiing may provoke eye rolling. But as Aspen goes, so goes any other mountain area. Aspen's leaders have come to grips with the fact that by the end of the century, there may be too little snow not only for skiing but for replenishing water supplies, sustaining fishing, and fighting fires, which would themselves be more frequent in water-starved forests. "When I first heard about this, I thought it was surprising," says Mearns, who participated in the Canary Initiative. "Little Aspen is going to do this full assessment? But as it went through, I realized this does make sense, because ultimately, mitigation on local

scales can help." Aspen may need to put ski lifts higher up the mountain and, eventually, plan for life after skiing.

If Aspen is, in its planning for climate change, an extreme exception at the local level, California is the exception at the state level; the California Energy Commission does more than any equivalent state agency to promote energy-efficiency technologies and renewable electricity sources like solar and wind. As a result, California's carbon dioxide emissions from power generation are, per capita, the lowest in the nation. But in the past three years, the energy commission's R&D effort has expanded to include studies of climate adaptation. A small portion of its annual climate budget, about $4 million, now goes toward regional computer modeling aimed at clarifying the implications of climate change for agriculture, forests, coastal management, and water supplies. "We want to know at higher resolution how the California snowpack and its water availability will be affected and, in turn, how agriculture and urban water-supply strategies may have to respond," says Martha Krebs, the commission's deputy director for R&D. "We need to know how sea-level rise and salt-water intrusion may affect coastal communities and what that will mean for city planning and development policy."

"We know the climate is changing, but they are managing the water system based on rules devised 50 to 100 years ago," says one researcher. "If what we project in the future is correct, we expect a pretty big problem." But technology that could guide better local planning is facing the budget ax.

Krebs anticipates that detailed regional models will, among other things, steer forest-management plans in new directions. California is considering the possibility that its forests could serve as "sinks" for carbon dioxide. One proposal is to reforest previously forested areas. But a hotter climate could stress existing plant species, and harsher droughts could leave these new forests more vulnerable to fire. The hope is that understanding the effects of climate change on California's complex topography and climatic zones will help foresters develop the right management strategies, including choosing specific trees that can survive harsh conditions.

California—battered by population growth, landslides, and water shortages—is already taking action on flood-control projects and considering how to protect, for example, freshwater intakes in the Sacramento River delta, which is expected to become more brackish. Now it's trying to respond specifically to climate change as well, but progress is slow. Coastal real-estate development policy, for example, hasn't changed. "How well prepared is coastal California to deal with the impact of climate change?" asked Susanne Moser, a coastal-zone expert at NCAR who is advising the state. "The bottom line is, there are very, very few counties and municipalities that are doing anything about this topic so far."

Staggering Backwards

On a wall-size screen inside the darkened Visualization Laboratory at NCAR, the display of global temperatures across two centuries gets rolling. The animation, which uses a middle-range estimate of future greenhouse-gas emissions, starts in 1870; small splotches of blue and yellow—minor temperature deviations from historical averages—flash over a slowly spinning earth. In the mid-1880s, more blues appear; the planet cooled for a time, thanks to atmospheric dust kicked up by the massive Krakatoa volcanic eruption in August 1883. Things level out at the turn of the century and remain steady through World Wars I and II.

But from the 1950s through the 1980s, yellow blotches proliferate. In the 1990s, the jaundice spreads; by 2005, the earth looks disturbingly like a glowing yellow tennis ball. By the 2050s, the top of the planet appears red. And by 2099, much of the world has been painted orange and red by global warming.

Another model shows the projected changes in seasonal expansion and contraction of Arctic sea ice as the years roll by. It's like a slowly diminishing heartbeat, with summer ice gradually vanishing.

Caspar Ammann, an NCAR scientist, offers some perspective on the disturbing show. A temperature increase at the upper end of the IPCC's projections—5 °C by the end of the century—is about the same size as the increase that's occurred since the depths of the last ice age. In other words, during the ice age, it was 5 °C cooler than it is today. If global temperatures rise 3 °C above recent averages, they will be in the vicinity of temperatures last seen three million years ago, when sea levels were at least 15 meters higher—though it could take centuries for ice sheets to melt and raise the oceans that much. "This is the magnitude of the [temperature] change that is possible in 100 years," says Ammann. "We need to see that perspective clearly."

Two days after I saw the NCAR simulations, I visited Ted Scambos, lead scientist at the University of Colorado's National Snow and Ice Data Center (NSIDC) in Boulder. Scambos studies ice dynamics to understand the rate at which

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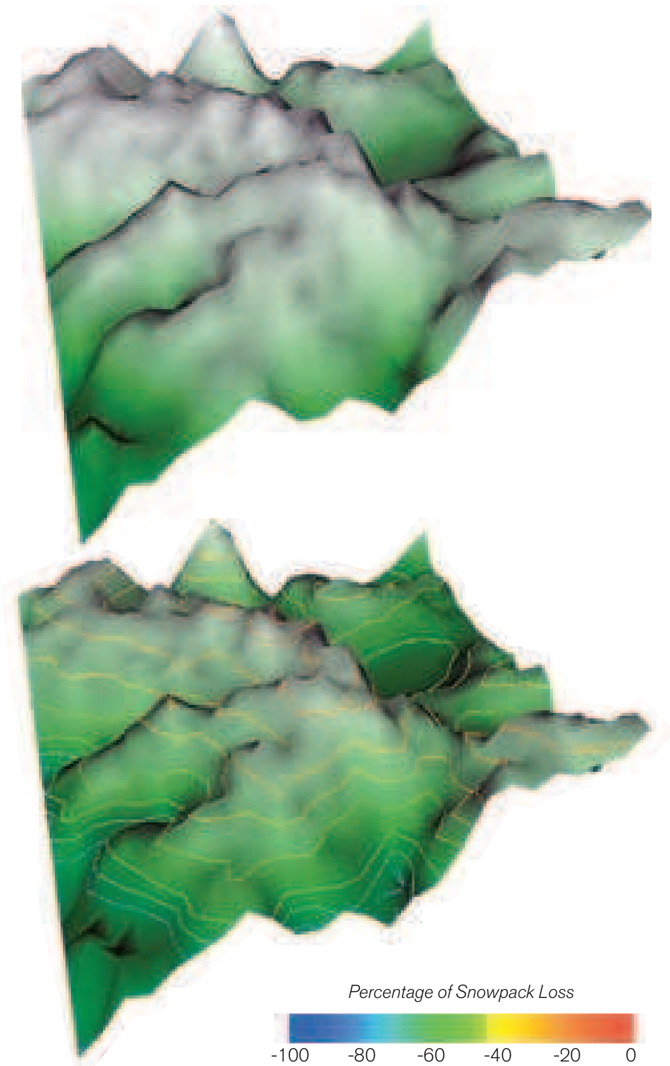


Vanishing Yosemite Snowpack

These images—which show details of the one on page 65—reveal snowpack changes in a 100-kilometer swath of California's Yosemite National Park. The top image shows current spring conditions, with snowpack depth depicted by colors (greener indicates less snow, whiter indicates more). The bottom image is a visualization of snowpack between 2050 and 2070. Contour lines depict percentages of snowpack lost, which range from 80 percent (light blue contour) near today's snow line to 20 percent (red contour) near peaks. This level of topographic precision is critical to helping communities plan for changes in the amount of annual snowpack and the timing of melting, on which millions of people depend for their water supplies.

COURTESY OF PACIFIC NORTHWEST NATIONAL LABORATORY

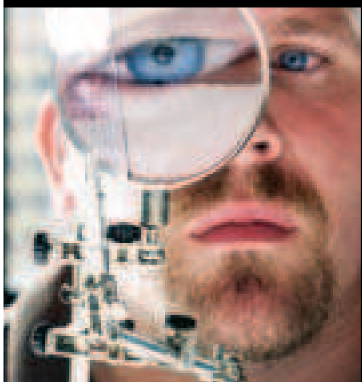
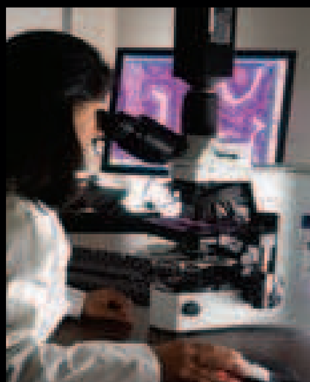
the ice sheets of Antarctica and Greenland are responding to climate change. He and other scientists at NSIDC spend their days poring over satellite data, studying how glaciers slide down ancient hidden fjords and how warmer ocean water and the glaciers' own meltwater lubricate their progress. "We are warming so fast that the earth is still staggering backwards from the warming," Scambos said. "We may have already crossed the threshold of the last warm period, a time when people were growing grain in Iceland and raising dairy cattle in southeastern Greenland. And even if you flattened out greenhouse emissions right now, my hunch is that all the arctic sea ice in summer will eventually disappear.

"We're really, really in trouble," he continued. "It's just a question of time. People say climate has changed before and people adapted. That is true. But there weren't six billion of us, with all the arable land working as hard as it could, and every one of those areas counting on climate more or less staying the same. All our infrastructure is built around this climate. Personally, I think we have a strong moral obligation to respond in a fashion that gives people a century from now a reasonable chance of making their way ahead. We should do something."

The ability to "do something," however, depends on getting information that is much better and more detailed. And that will depend on increasingly precise computer models and more monitoring equipment to feed data into those models. Not every city has a Goddard Institute for Space Studies in its backyard, Cynthia Rosenzweig points out. She says every local government should be given the tools to understand how global warming will affect its community. "We need a national capacity for scenarios, to provide every locality in the nation with the input variables they need for projecting impacts and preparing adaptations," she says. "We should begin to incorporate sea-level rise into plans for coastal development. We should improve our responses to heat waves—now—so we can be prepared for greater frequency and duration. And we should consider the potential for more droughts—how we would manage for more droughts and floods."

But from NASA to the NOAA to the National Science Foundation and the U.S. Department of Energy, the budget picture is dismal. In 2005 dollars, the annual federal budget for climate-change research has been slashed from more than $2 billion in the mid-1990s to less than $1.6 billion today. Earlier this year, a National Academy of Sciences report warned that Earth-observing satellites—basic hardware for monitoring climate change—were at "great risk" of blinking out. Without urgent investment, the report warned, 40 percent of sensors and other instruments aboard NASA spacecraft could stop functioning before the end of the decade. "At these agencies, earth-science and climate-science budgets are either level or decreasing in real dollars," says MIT's Ronald Prinn. "Under those circumstances, what is needed for helping out states and cities is just not going to appear. It is a sad state of affairs. At a time when we should be trying to help at the regional to the local level, with sound advice, we are facing this incapability to have accurate forecasts at the local level that make the advice worth taking." TR

David Talbot is Technology Review*'s chief correspondent.*


Sequencing in a Flash

A new generation of DNA-sequencing machines is opening up whole new areas of genomic research. Already, researchers are unraveling how modern humans differ from Neanderthals and devising more precise tests for cancer.

By Jon Cohen

On February 6, 2007, executives from 454 Life Sciences showed 78-year-old James Watson a first draft of his own genome. There was something downright poetic about this. Watson, of course, had won a Nobel Prize 45 years earlier for his role in discovering the double-helical structure of DNA; he was also a prime mover behind the Human Genome Project, which by its completion in 2003 had spent nearly $3 billion over 13 years extracting the blueprint that those helices encode. Now 454 had moved a step beyond that megaproject, which pooled many people's DNA to determine the genetic sequence of what amounts to a model human. The company and its so-called next-generation sequencing machine had single-handedly read the genetic code of an individual—one whose work had done so much to make the achievement possible.

But Jonathan Rothberg, who founded 454 in Branford, CT, with the dream of producing a sequencing machine more efficient than those available to the Human Genome Project, does not mention poetry when he recounts his meeting with Watson. Rather, he talks about money, speed, and a future in which ordinary people carry around their personal genomes on discs—an increasingly plausible scenario. "It cost us $200,000 to do Jim Watson," points out Rothberg. "And we did it mostly in December and January."

Rothberg, who now chairs 454's board of directors, emphasizes that "Project Jim" remains a work in progress and will require more time and money. As of February, the company had sequenced Watson's DNA only three times (each run increasing accuracy and filling gaps); nine passes were required to produce the Human Genome Project's final draft sequence. But still.

Rothberg's company is just one of several, including Illumina of San Diego and Applied Biosystems of Foster City, CA *(see "Other Advanced Sequencers," p. 74)*, developing machines that can decode DNA faster than ever before. And just as the cost of computer power has plummeted with the steadily increasing density of transistors on chips, the price of sequencing DNA has fallen rapidly with the advent of these machines. Today, the price tag on a human genome decoded with sequencers of the type used in the Human Genome Project would be $25 million to $50 million. It drops to around $1 million with next-generation machines available today and could be as low as $100,000 by 2008.

As the history of computers has shown, more processing power for less money can lead to unanticipated applications. In the wake of the Human Genome Project, researchers faced difficult financial decisions about which genomes to sequence next: chimpanzee or macaque, cow or dolphin, rice or cassava. The new machines make it possible to sequence nearly everything of interest. And as ever more sequence data flows into databases, whole new areas of research are opening up. Scientists now have an unprecedented ability to make comparisons between species, shedding light on everything from evolutionary questions to genetic reasons for individual differences in disease resistance and susceptibility. Research done with 454's machines and published in top journals includes the partial sequencing of a Neanderthal genome and the development of new

STEVE MOORS

454's Jonathan Rothberg believes his machines will make sequencing so cheap and fast that it will become practical to read the genomes of individuals.

tests for cancer-causing genetic mutations—technology that may help doctors tailor treatments to their patients.

"The last year has been the most exciting period in genomics since the days of the Human Genome Project," says Eric Lander, first author on the project's first published draft of the human genome and now head of the Broad Institute for genomic medicine in Cambridge, MA. "Sequencing is becoming cheap enough and powerful enough that it can be applied to about any problem. It's standing the field on its head." Francis Collins, who led the Human Genome Project for the National Institutes of Health, predicts that the new sequencing technologies "will have profound consequences for the future of biomedical research and, ultimately, for the practice of medicine."

A Unique Solution

Jonathan Rothberg's office has a diner theme, with a red-and-black checkerboard tile floor, red Naugahyde-covered chrome chairs, and a sofa with arms that imitate the rear of a 1959 Cadillac, complete with monster tail fins and bullet-shaped taillights. Instead of a desk, he has a diner bar with bar stools. Wine bottles from a Connecticut vineyard he owns line some of the shelves. Beyond the windows lies the Long Island Sound. The place screams *I am unique*. And so Rothberg is. In 1991, while completing his PhD in biology at Yale University, he started CuraGen, one of the first companies to develop drugs based on genomics. In addition to CuraGen and 454 Life Sciences, he has founded an institute for the study of childhood diseases and yet another biotech company, RainDance Technologies, which has developed what it calls "liquid circuit boards" that are designed to make experiments more efficient by manipulating tiny quantities of fluid. And all that by the age of 43.

Indeed, it was an interest in the uniqueness of each person that ultimately led him to try to design a sequencer that he hopes will one day make genome checks as routine as blood tests are now. Rothberg holds up the guts of the 454 machine, a glass slide with 1.6 million miniature wells, each approximately 50 micrometers wide (about half the width of a human hair) and 55 micrometers deep. It is this chip that allows the machine to sequence DNA so quickly, because a separate chemical reaction can be carried out in each well.

Gene sequencing takes advantage of the fact that the two strands of a DNA helix are complementary: of the four chemical "bases" adenine, guanine, thymine, and cytosine, which are strung together in various orders on each strand, adenine pairs only with thymine, and guanine only with cytosine. In the most commonly used sequencing technique, which builds on a scheme developed 30 years ago by the University of Cambridge's Frederick Sanger, fragments of DNA are separated into single strands and exposed to free nucleotides, which bind to the original As, Cs, Ts, and Gs to generate new complementary strands. These strands vary in length because some of the free nucleotides have been modified to prevent the reaction from continuing; when one of these bases binds to its target, the chain stops growing. And each of these four types of chain terminators has a different fluorophore attached that fluoresces when struck by a laser beam. An electric current separates the strands by size, and the laser reads the colors to determine which was the last base added to each chain, spelling out the sequence. The vast majority of labs that do sequencing today use a machine made by Applied Biosystems that spits out about two million bases a day.

The latest sequencer from 454 can read 300 million a day.

The 454 method avoids several of the more time-consuming steps of conventional sequencing, such as the separation of strands by size. Unlike Sanger sequencing, it doesn't terminate chains: it records bases as they're added to a growing strand. First, a DNA molecule is randomly chopped into different lengths. Then each fragment is stripped into single strands, and each strand is attached to a separate tiny bead. A biochemical process copies the single strands, so that 10 million clones jut out from each bead. Each bead is then packed into one of the 1.6 million wells. As, Cs, Ts, and Gs wash over the wells sequentially to synthesize new complementary strands.

Here's the truly clever part: using a method first described by Pål Nyrén and coworkers at Sweden's Royal Institute of Technology, 454's sequencer instantly records when a base is added to each strand by exploiting the fact that the binding reaction releases a chemical called a pyrophosphate. In the wells of the 454 machine, the pyrophosphate is captured by a chemical cascade that ends up flicking on the enzyme luciferase (which occurs naturally in fireflies)—emitting a burst of light. A standard charge-coupled device of the kind used in digital cameras and telescopes detects each flash, reading off the sequence

Other Advanced Sequencers

Company	Approach	Status
Illumina, San Diego, CA	Synthesis and fluorescence labeling	Commercialized
Applied Biosystems, Foster City, CA	Ligation and fluorescence labeling	Scheduled for mid-2007 launch
Helicos BioSciences, Cambridge, MA	Single-molecule sequencing without amplification	Scheduled for late-2007 launch

of As, Cs, Ts, and Gs in each fragment. The process can read about 200 to 300 bases in a row. As in conventional sequencing, computers then look for matching sequences at the end of one fragment and the start of another, piecing the fragments back together in the correct order.

The sequencer that 454 brought to market in October 2005 had a few serious limitations. It could read only 100 bases in a row (the longer the stretch of bases in each sequenced fragment, the easier it is to assemble a complete genome), and it also had trouble accurately mapping repetitive stretches—say, six As back to back. But Rothberg says 454's philosophy was "Get it out early; get it accepted." The company first targeted "early adopters" like Broad's Lander, hoping they would soon publish findings that relied on the sequencer. "You've got to get early guys first, but the rest of the guys, the followers, are where the market is," says Rothberg. "And they read peer-reviewed papers."

While it's impractical to use conventional DNA-sequencing methods to sniff out the differences between, say, a tumor cell and a person's healthy cells, the next-generation sequencing machines can perform such experiments easily and cheaply.

Neanderthals

One paper by an early adopter that received widespread attention from scientists and the public alike was a study of Neanderthal DNA led by Svante Pääbo of the Max Planck Institute for Evolutionary Anthropology in Leipzig, Germany. Neanderthals, the closest species to modern humans, disappeared some 30,000 years ago, and more speculation than fact surrounds their genetic relationship to us. Though Pääbo had done some previous studies with Neanderthal DNA, anything beyond rudimentary analysis had proved too difficult and costly. The problem is that over thousands of years, the few known samples of Neanderthal DNA from fossils have been degraded to short fragments of around 50 to 75 base pairs. In addition, the DNA is often contaminated with genetic material from microörganisms and the modern humans who have handled the fossils. But Rothberg believed that the 454 machine could analyze many short sequences at little cost, generating enough information to let scientists sift ancient treasures from junk. Rothberg cold-called Pääbo, who agreed to collaborate.

After sequencing genes from 70 Neanderthal bone and tooth samples, Pääbo's team and researchers from 454 found one sample, estimated to be 38,000 years old, that had mostly clean DNA. As they reported in a paper published last fall in *Nature*, they then sequenced one million base pairs from less than 200 milligrams of material, an achievement that has yielded clues about whether modern humans and Neanderthals interbred and when the two species diverged from each other. More important, the paper shows that sequencing all three billion bases in the Neanderthal genome is feasible. Doing so could help solve such mysteries as whether Neanderthals had the genetic ability to speak.

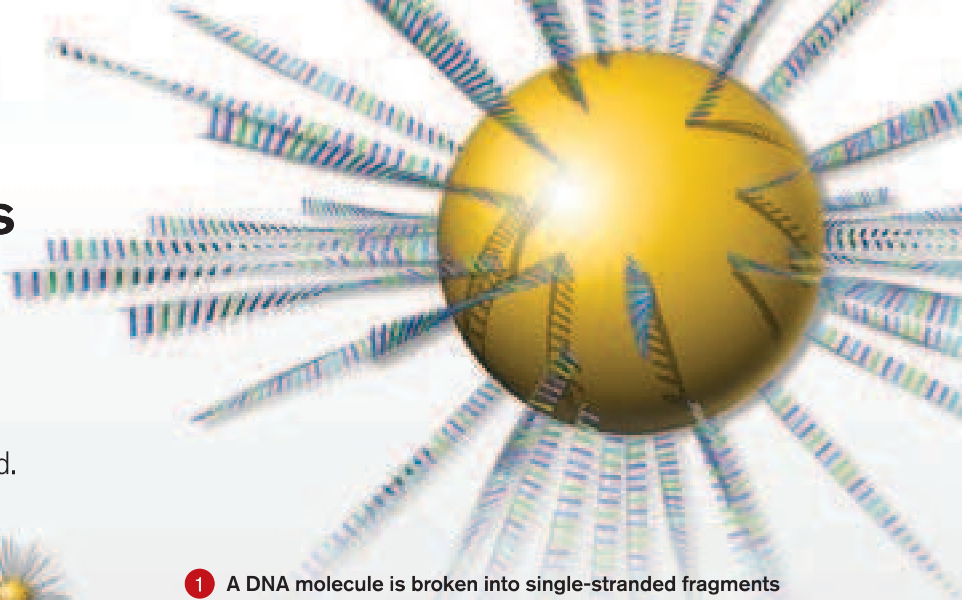
Sorting out whether humans and Neanderthals interbred or even had the capacity to talk to each other may get a lot of press and public attention, but other applications for ultrarapid DNA sequencing could have a far greater impact on medicine and on our lives. The traditional sequencing method looks at DNA from many different cells. But if one of those cells is, say, a tumor cell, its sequence can differ slightly from those of the healthy cells. In such cases, the computers select the sequence that's most commonly found and discard the others. Next-generation sequencers like the ones marketed by 454 instead clone and sequence single molecules of DNA, allowing "ultradeep" probing that can unearth rare variants. (Traditional sequencers can also analyze single molecules, but it's prohibitively expensive.) The implications of single-molecule sequencing are enormous for medicine. While it is not practical to use conventional sequencing to sniff out the DNA differences between healthy and diseased cells, the new machines can perform such experiments easily.

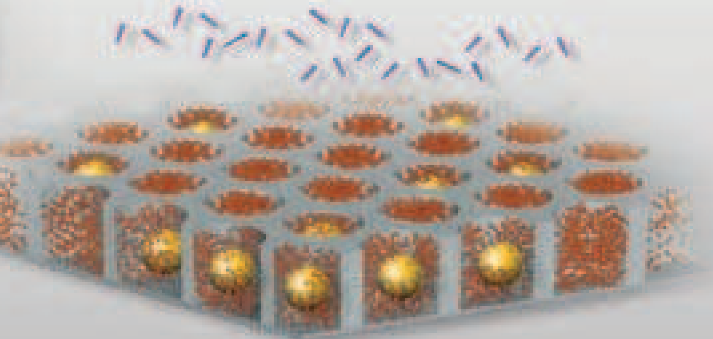
Matthew Meyerson, a clinical pathologist at the Dana-Farber Cancer Institute in Boston, has published a study showing how the 454 machine can help uncover mutations linked to lung cancer. Lung-cancer drugs now available target the gene that Meyerson is sequencing, and he hopes that physicians will ultimately gain a better handle on who will respond to which drugs by learning whether the patient has a particular mutation. "I imagine in a few years all cancer patients will have their tumors characterized by single-molecule sequencing if the technology continues to decrease in cost," he says.

In a variation on this theme, Michael Kozal, an AIDS clinician at Yale, has joined with 454 to do ultradeep sequencing of HIV to determine the presence of minor populations of drug-resistant virus. Early tests of the technique in patients detected about twice as much resistant HIV as Sanger sequencing did. This information, too, could help physicians individualize treatment regimens, which would increase cost-effectiveness. "It's practical to do in our system," says 454 chief scientist Michael Egholm, who is collaborating with Kozal. "Before, it simply wasn't affordable."

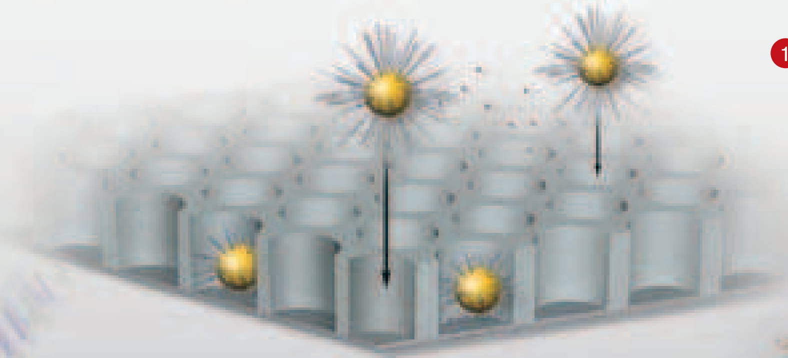
Sequencing Secrets

Using a strategy significantly different from the one used in conventional sequencing, 454's machines are able to read 300 million DNA bases a day. The key is a massively parallel approach that can be easily automated.



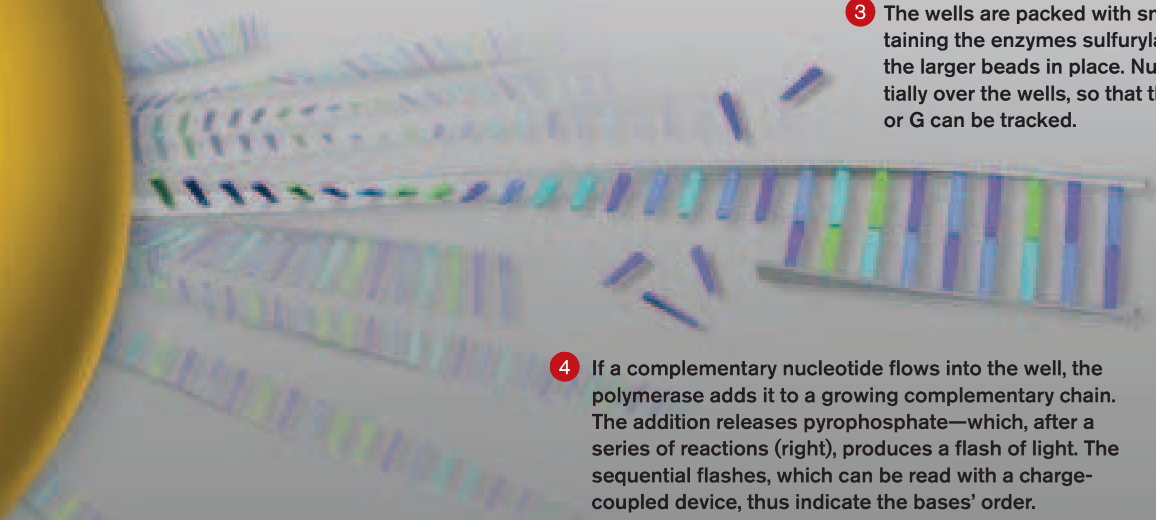


1 A DNA molecule is broken into single-stranded fragments 200 to 300 bases long, which are attached to tiny beads. The fragments are then cloned, so that millions of identical copies of them cling to each bead (above). The DNA is now ready for sequencing.

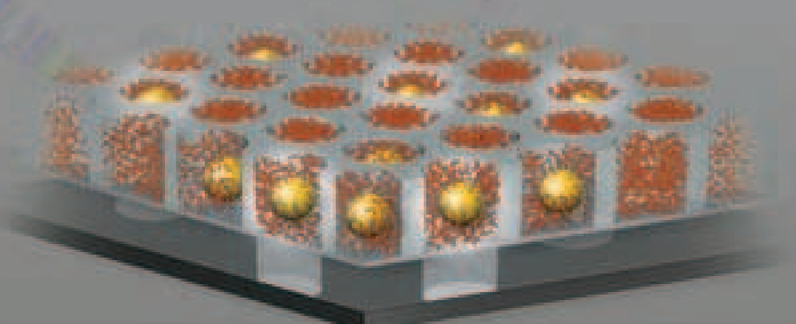


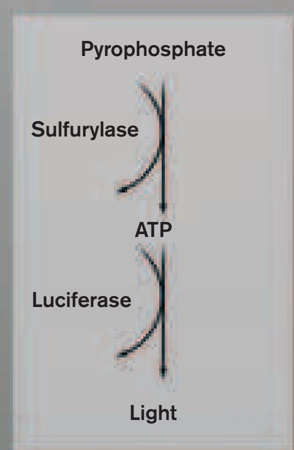
2 The DNA-studded beads are mixed with polymerase and loaded into a plate with 1.6 million wells. The small size of the wells ensures that only a single bead will be deposited in each.

3 The wells are packed with smaller beads (in red) containing the enzymes sulfurylase and luciferase, holding the larger beads in place. Nucleotides then flow sequentially over the wells, so that the addition of each A, C, T, or G can be tracked.



4 If a complementary nucleotide flows into the well, the polymerase adds it to a growing complementary chain. The addition releases pyrophosphate—which, after a series of reactions (right), produces a flash of light. The sequential flashes, which can be read with a charge-coupled device, thus indicate the bases' order.





MyGenome

George Church, a sequencing pioneer at Harvard Medical School, says cost is the key. As their prices fall in the next few years, he says, these machines will become a democratizing force that will make traditional sequencers all but obsolete, much the way personal computers displaced mainframes. And this will lead to applications that no one can yet fathom. "If we were still working with mainframes, a lot of cool stuff wouldn't be happening," he says.

Church, who was among the dozen researchers to propose the Human Genome Project in the mid-1980s, is one of the few biologists whose lab equipment includes a table-mounted vise grip and a drill press. He uses equipment like this to build his own next-generation sequencers, of which his lab currently has eight *(see TR35, September/October 2006)*. Convinced that companies are overcharging for their machines, he makes a point of freely sharing his know-how with any interested colleagues. He compares his philosophy to the "wiki and Linux mentality," saying, "If a bunch of ants get together, they can move a rubber-tree plant."

Church's grand vision is to channel the cheap flood of As, Cs, Ts, and Gs into what he calls the Personal Genome Project. In the Human Genome Project, researchers obtained DNA from several people, each of whom, for privacy reasons, remains anonymous. So the final sequence represents a composite person with a conglomerate of different genetic backgrounds and medical histories. Church wants his Personal Genome Project to decode the DNA of individuals, who will also volunteer their medical records. He will post all the resulting data on the Internet. Ultimately, he imagines, millions of people will join the project, posting their sequences, medical records, and, if they choose, even facial photographs online. The entire world will then have access to all the data it needs to freely test hypotheses.

Although Church has received substantial funding from the National Institutes of Health to develop sequencing technology, the ethical, legal, and social questions raised by the personal Genome Project have kept NIH from supporting it, despite a positive review of a grant application in August 2005. "As soon as I got approval, NIH got all excited, and not necessarily in a good way," he says. He's attempted to address the privacy and confidentiality issues, noting that no one's identity needs to be made public and that NIH already funds human genetics projects that have fewer safeguards in place.

Church recognizes that intimate knowledge of their own DNA might be too much for many people. "You don't let your kids browse to Internet pornography sites," he says, "and to some extent you don't allow yourself to browse the scariest, grossest sites." He expects that rather than accessing their raw genomes, people will have professionals help them interpret the information.

TAMI TOLPA

Despite the lack of federal funding and the ethical objections, Church is proceeding, confident that advances in sequencing technology will drive the idea of a Personal Genome Project forward—just as advances in information technology have led strangers to share data in ways that no one dreamed of when the dual-floppy-drive Apple II debuted 30 years ago. As sequencers become more efficient, he believes, and costs continue to drop, personal genomics will take off on a scale that few people have yet imagined.

Winning the Lottery

Last October, the X Prize Foundation announced a $10 million award for producing highly accurate sequences of 100 human genomes in 10 days or less without spending more than $10,000 per genome. One of the first entrants was 454, which plans to develop even smaller beads that it hopes will allow its machines to read even more DNA per run at roughly the same cost. "We don't need any new physics or math to get to the $1,000 genome," says Rothberg.

Leaving aside the question of when—or if—anyone will claim the X Prize, DNA sequencing will surely continue to plummet in price and increase in accuracy. "Until last year, sequencing was really struggling to have the impact on the next era of genomics that it needed to have," says David Bentley, Illumina's chief scientist. Basically, the price of traditional sequencing was just not dropping quickly enough. "Now the field is far more optimistic than it was," he says. Next-generation sequencing "has a huge role to play."

Hearing scientists tick off the possibilities is like listening to lottery winners. And personalized medicine like the type of cancer testing and treatment that Dana-Farber's Meyerson hopes to help usher in is just a starting point. Bentley says the new sequencers will open windows on the vast "noncoding" regions of the genome that turn genes on and off. Egholm of 454 notes that the Human Genome Project did not actually sequence every last bit of human DNA; there may still be undiscovered genes that additional sequencing can find. Broad's Lander imagines a torrent of new information about what leads a cell to differentiate into one type or another (a central mystery in developmental biology) and what controls different cellular states. "I realize that's harder to explain than curing cancer," he says, "but it's ultimately more important, because it will affect all diseases."

Within the next year, Lander predicts, scientists will be able to begin studies that generate "terabases" of information—one trillion As, Cs, Ts, and Gs. "I never even spoke the word *terabase* before last year," he says. "And if all those data are on the Web and freely available, it's going to drive a completely different kind of biology." TR

Jon Cohen, a San Diego–based freelance writer and correspondent for Science, *is working on a book that looks at the genetic differences separating chimpanzees from humans.*

Essay

The Trouble with Knowledge

Technology that alters human nature will upset our inherited moral categories, argues one of Britain's most esteemed philosophers. In a posthuman future, he asks, how will our children and grandchildren know right from wrong?

By Roger Scruton
Illustration by Sam Weber

In his novel *Erewhon*, published in 1872, Samuel Butler describes an imaginary country (a "nowhere") in which all machines are forbidden. The inhabitants had once availed themselves of watches, steam engines, mechanical pumps and hoists, and all the other devices that could be admired in the great exhibitions of Victorian England. ¶ But unlike Butler's Victorian contemporaries, they had perceived the terrible danger that these things represented. Machines, they realized, were always improving. Never for one moment did they take a step backwards into imperfections that they had surpassed. Always, the next machine was better, more versatile, and more fully adapted to its uses than the last.

Inevitably, therefore, the process of improvement would continue, until machines had no need of humans at all—until they were able to produce and reproduce themselves. At that point, like all creatures obedient to the law of evolution, the machines would be locked in a struggle with their competitors. Their only competitor would be man. Hence, foreseeing that the machines would otherwise destroy them, the inhabitants of Erewhon had destroyed the machines.

The fear of the Erewhonians was not irrational; but its premise was unconvincing—at least to Butler's readers. The idea of a self-reproducing machine seemed, to most of them, a mere literary fantasy. Sixty years later, however, Aldous Huxley published *Brave New World*, the portrait of another imaginary country, in which humans are produced as machines are produced, according to specifications laid down by official policy. Intelligence, interests, pleasures, and pains are all controlled, either genetically or by conditioning, and all those aspects of the human psyche in which eccentricities, commitments, deep emotions, and virtues might take root are deliberately prevented from developing. And if humans can be produced as machines are produced, in factories controlled by humans, why cannot machines be produced as humans are now produced, by self-reproduction?

Scientific advances had made Huxley's prophecy rather more plausible than Butler's. But if Huxley's readers felt a chill of apprehension, it was for another reason than any Erewhonian fear of machine rule. The world described by Huxley is one that has crossed a moral barrier. Even if the Erewhonians were right to fear the machines, and even if they had let the machines develop to the point of danger, they themselves would not have been changed by this. In any future crisis, their sense of solidarity, duty, and heroism could be marshaled in their own defense. Human nature would have remained—a fixed point in their universe, the premise from which all their practical reasoning began. But suppose human beings become a laboratory product, as Huxley envisaged. What then remains of human nature? Where is the fixed point, the thing that cannot be touched, the thing beyond choice, for the sake of which all choice is undertaken?

That is a loaded way of putting it. But it captures, I believe, the growing fear in our society of scientific

advance, and in particular the fear of genetic engineering and the possibilities that it opens to us. As science advances, bringing nearer and nearer the day when Jill can be designed by Jack for uses of his own, many people are beginning to share Huxley's anxiety. Technology, they fear, will imperil human freedom. One generation will be able to assert what the bioethicist Leon Kass has called a "genetic despotism" over the next, and gradually, as human nature is transformed in accordance with our own designs, the point and value of life will slip from our grasp.

'Twas Ever Thus

The problems of biotechnology are in one respect like the problems of any technology. All discoveries, however beneficial, have unwanted side effects, and any technology can be used to good or bad ends. Hence there is no technological advance that is not greeted, at some stage, by protests. History does not record the protests that surrounded the invention of the wheel. But it certainly records the protests that surrounded the invention of the railways. For the great critic and social philosopher John Ruskin, the railways were a ruthless assault on rural tranquility: they destroyed the sense of place, they uprooted settled communities, they overran the countryside with steel-clad ugliness and urban sprawl. They set us all in motion, when the true point of human life, Ruskin thought, was to stay quietly where we were. Oddly enough, the railway bridges and stations of England were built according to aesthetic principles influenced through and through by Ruskin's writings, and in particular by *The Stones of Venice*; they are looked back on now with intense nostalgia, as symbols of peace, place, and distance. And campaigners against automobiles adduce railways as their ideal of a safe, environmentally friendly, and aesthetically pleasing link from place to place across a continent.

Even if Ruskin's protest against the railways has lost its persuasive force, it belongs to a habit of mind that is one of our deepest instincts. For Ruskin, the railways threatened one of the fixed points in our moral universe, which was the earth itself—the earth that provides the food we eat, the water we drink, and the stones with which we build. There is a natural way of using the earth, which is to respect it as our home. When we build, we must treat the land as a place of settlement, into which our lives are harmlessly slotted like those of fish in the sea. In a similar vein, contemporary environmentalists complain that by exploiting the earth for our ephemeral purposes, we treat as a means what should be respected as an end.

Like Ruskin, environmentalists who lament the costs of present knowledge tend to forget the costs of former ignorance. Burning wood caused the deforestation of Europe, the desertification of North Africa, and the drying up of lakes and rivers all over the Middle East. This was an environmental catastrophe, which could have been prevented had the Romans and other ancients known what we know about soil erosion, microclimates, and the chemistry of carbon. The environmental problems that we confront today are not going to be cured by returning to old ways of life or old ways of extracting energy. It is not technology that has caused our environmental problems but *incompetent* technology—technology that has failed to address the real question, of how to extract energy without damaging the planet. As Butler might have said to the inhabitants of Erewhon, Don't destroy the machines; let the machines take over. But first make sure they are correctly programmed.

However, that response does not get to the heart of the current anxiety. Our desire for a controlled environment wars with our sense that some things ought to be beyond our control—things like the tides, the seasons, the movement around us of the elemental forces on which we depend. To attempt to bring them under control is, we believe, to challenge fate, whose only law is the law of unintended consequences.

The "I" and the "We"

There are two contrasting attitudes that we take toward practical questions, which we might call the "I" attitude and the "we" attitude. As a rational agent, I see the world as a theater of action, in which I and my goals take a central place. I act to increase my power, to acquire the means to realize my objectives, to bring others to my side, and to work with them to overcome obstacles. This "I" attitude is implanted deep in the psyche, since it defines the starting point of all practical reasoning and contains an indelible intimation of the thing that distinguishes people from the rest of nature—namely, their freedom. There is a sense in which animals, too, are free: they make choices, do things both freely and under constraint. But animals are not accountable for what they do. They are not called upon to justify their conduct, nor are they persuaded or dissuaded by dialogue with others. This strange feature of the human condition has puzzled philosophers since Aristotle; and it is the foundation of all that is most important to us. All those goals that make human life into a thing of intrinsic value—justice, community, love—have their origin in the mutual accountability of persons, who respond to each other "I" to "I."

Behind all my projects, however, like a horizon against which they are projected, is another and quite different attitude. I am aware that I belong to a kind, and that kind has a place in nature. I am also aware that we are part of a world to which we are adapted. Whereas the "I" attitude seeks change and improvement, overcoming the challenges presented by nature, the "we" attitude seeks stasis and accommodation, confirming that we and our world are at one. Things that threaten the equilibrium between human beings and our environment, either by destroying that environment or by undermining human nature, awaken in us a profound sense of unease, even of sacrilege. The "we" attitude tells us that we must never disturb the two fixed points of our universe, the environment and human nature. This attitude may be the residue of prehistorical events, an unconscious memory of the original harmony between "our hunting fathers" and their natural home, from which our species departed on its journey into knowledge. But it continues to exert its influence on our practical reasoning, filling our minds with ideas of a prelapsarian innocence.

It will be objected that human nature does not stand still. The "I"' attitude restlessly pursues the path of invention, and in doing so radically changes the focus and the goal of human conduct. Consider television. Here is a technological achievement that has changed our world. It is a source of pleasure to billions and a channel of instruction and information that keeps people comfortably entertained at home when they might otherwise have been outside fighting. Such, at least, is the good side of it. But as with so much technology, there is a bad side too. The physical effects of television, in the form of obesity, heart disease, and general apathy, are observable everywhere. So too are the mental effects: the shortened attention span, the inability to comprehend abstract arguments, the exaggerated appetite for visual stimulus, the enhanced aggression when dealing with ordinary things, and the debilitating addiction to the very thing that causes those faults, which is the moving image on the screen. All this has been well documented (and in "Television Addiction Is No Mere Metaphor," an article in the February 2002 *Scientific American*, Mihaly Csikszentmihalyi and Robert Kubey make a stab at identifying the neurological cause of the addiction). Those of us who take due note of the arguments will, drawing on our vision of human nature and of the capacities and virtues required for its fulfillment, control our children's viewing times, try our hand at programming the machine with TiVo or a built-in censor. Failing that, we will revert to the Erewhonian solution and do as my father did when, after an elevating speech about the damage we humans inflict on ourselves by absorbing passively the entertainment that we should be creating actively, he tossed the thing through the window and then ran down the stairs to finish it off with a hammer.

The change in human nature that has come from television is, however, both small and manageable. We can deal with it through our old moral and prudential categories. Children raised on television can understand one who tells them that there are other and better forms of entertainment; there are clear examples of "conversion experiences," in which addicts suddenly and definitively turn the thing off. Television has not led us to revise the list of human virtues so as to include apathy and voyeurism, or to downgrade the appeal of courage, justice, and self-sacrificing love. All in all, it leaves our vision of happiness unaltered. True, it has proved to be no more than a stepping stone toward other and more radical forms of entertainment and communication. But, we are apt to feel, it is best to accept these technological advances, to take comfort in the ability of human beings to adapt to them, and to incorporate them into new forms of community and new ways of reaching out to our kind. For the kind hasn't changed, nor have its needs *(see "Literacy and Text Messaging" on technologyreview.com)*.

... after an elevating speech about the damage we humans inflict on ourselves by absorbing passively the entertainment that we should be creating actively, he tossed the thing through the window ...

But this returns me to Huxley's dystopia. As Huxley foresaw, the same easygoing attitude cannot be taken in the face of those technological developments that bring human life itself within our power. From the moral point of view, biotechnology is inherently problematic. It is not simply that the research needed to develop its techniques involves the manipulation of living things, both animal and human, in ways that some would regard as immoral. It is that the techniques themselves are inherently subversive. Like other technical advances, they can be applied to the benefit of human beings and also to their harm. But however they are applied, when they are applied to *us*, they alter us in ways that affect our conception of what we are. Since our moral opinions

derive from our conception of human nature, this alteration leaves us disoriented, without the capacity to judge the right and wrong of what we do. Some welcome this development, believing with Nietzsche that human nature must be transcended, into a world "beyond good and evil." For others, however, Nietzsche's prophecy of the *Übermensch* and his postmoral world should serve as a warning. For such people there is a perceived need for the President's Council on Bioethics, whose mission is "to undertake fundamental inquiry into the human and moral significance of developments in biomedical and behavioral science and technology."

Whichever line we take, we must recognize that we are at a turning point in our ability to alter our biological nature. We already have powers to prevent fertility and also to promote it. We can initiate life in a laboratory, and nurture it in vitro. We can screen for genetic disorders in embryos and decide from the results whether they ought to survive *(see "Picking the Best Embryo from the Bunch" on technologyreview.com).* We can insert new genes into parts of the adult body and will soon be able to insert them into gametes and embryos. There is hope, as the fertility expert Robert Winston suggested in his Alfred Deakin Lecture in Melbourne on May 13, 2001, that we might engineer the removal of the gene that causes beta thalassemia (a form of anemia)—a gene carried by one out of seven Sardinians. We can replace body parts with artificial versions, and we can transplant organs from one body to another. We can wire computer chips into the body—and maybe soon into the brain, to enhance memory or even intelligence. We are on the verge of a stem-cell therapy that could reverse some forms of blindness *(see "Using Stem Cells to Cure Blindness" on technologyreview.com).* All such developments both fascinate and alarm us. They promise relief from degenerative diseases. But they also undermine that "fixed point" on which the "we" attitude is focused, the fixed point of human nature—the fixedness of which was safeguarded by traditional religion in the doctrine that we are created in God's image and are therefore as unchangeable as He.

The Anxiety of Age

Human anxieties are never more vividly felt than when we contemplate old age. In earlier times, when it was generally assumed that human life had a divinely ordained span of threescore years and ten, when doctors did not reproach themselves when their octogenarian patients died, and when the scarcity of medical resources meant that the young had precedence in the use of them, old age was not an ethical problem. Cures that increased the chances of a long life were accepted as unquestionable benefits. And the old Hippocratic oath, by which doctors dedicate themselves to the goal of restoring health and refuse to harm their patients, seemed sufficient to resolve the occasional moral dilemmas. Joint replacements, organ transplants, and the possibilities of stem-cell therapy (to name just a few techniques) have changed all that. Old age is fast becoming a disease in its own right, and one that can be prolonged far beyond the previously recognized norms. Old people can be kept alive with spare parts donated by or purchased from younger people. One day, in the not-too-distant future, they will be patched up with stem cells taken from embryos. And with each medical advance, new ways of dying reveal themselves, along with new ways of being an unutterable nuisance to others. As biotechnology goes on postponing the day of reckoning, old age becomes an ever more visible reality among us—to the point where, in a few decades, there will be whole societies in which the majority are over 50 years old.

The second law of thermodynamics, which tells us that entropy is always increasing, seems to imply that all systems will randomize in the long run, ourselves included, and therefore that the right thing is to accept old age and its attendant ills with whatever serenity we can muster. We can more easily do this if we follow our ancestors and associate aging with wisdom and dignity. By pursuing wisdom, old people make themselves useful to the young and so ensure the only kind of earthly afterlife that matters, which is the affectionate memory of those who are not yet dead. So people used to think, at least; but Aubrey de Grey, a highly controversial self-described "theoretical biogerontologist," will have none of it. The answer to the moral problems of longevity, he believes, is to replace longevity with indefinite life, so that we all have the chance to be eternally young. De Grey's obsessive pursuit of the elixir of eternal life, which was described by Sherwin Nuland in the February 2005 issue of this magazine, must surely represent an extreme case of technological confidence. Decay, de Grey argues, is reversible: import enough energy into a system and order can be indefinitely preserved. In the case of aging, this requires us to reverse all the processes that lead to the collective suicide of a colony of human cells. A tall order, perhaps, but not one that we can rule out *a priori.*

What if de Grey's project succeeds? The "I" attitude rejoices at the thought of immortality; but the "we" attitude prompts us to hesitate. Imagine a world in which every human being, barring accidents, could stay around forever. If the planet were to bear the

weight of its immortal passengers, their numbers would have to be strictly limited. Reproduction, beyond a certain point, would have to be ruled out. Resources would have to be precisely allocated and scarcities avoided. For these eternal beings would be dangerous—and especially to each other. They would have worked out ways to exert and survive aggression, and these abilities would put them way ahead of any mortal competitors—ahead of everything save themselves. Life among the immortals would be scary beyond belief; its possibility would depend on a rigorous system of totalitarian control, which would forbid the ordinary forms of human happiness, not least the bearing and loving of children. Hardened by centuries of cynical dealings, the joyless predators would prowl around each other, seeking the small, spare advantages that are the only things worth aiming at in a world where everything is allocated by a committee of immortal enforcers.

The Moral Confrontation

Now, it is not as though the world of art and literature has been silent on this issue. Poetry, drama, painting, and music show us that mortality is inextricably woven into the human scheme of things; that our virtues and our loves are the virtues and loves of dying creatures; that everything that leads us to cherish one another, to sacrifice ourselves, to make sublime and heroic gestures, is predicated on the assumption that we are vulnerable and transient, with only a fleeting claim on the things of this world. On such grounds Leon Kass has argued for what he calls the "blessings of finitude"—for the intimate connection between the things that we value and the fleetingness of life.

That is not how Aubrey de Grey sees the matter. He told Nuland that "the right to live as long as you choose is the world's most fundamental right." De Grey silences all moral qualms about his mission by affirming his belief that he has a moral *duty* to proceed with it. What greater benefit can be offered to humanity than the benefit that overcomes the curse of Adam and vanquishes our greatest fear? As for future generations and the love of children, in de Grey's view reproduction has until now been simply the "done thing," the result of indoctrination into values that will have no place among the immortals.

De Grey argues that we have a moral duty to provide people with the choice as to how long they will live. Sherwin Nuland rightly protests that "as with every other of his formulations, this one—the concept of untrammeled freedom of choice for the individual—is taken out of the context of its biological and societal surroundings. Like everything else, it is treated in vitro rather than in vivo." But then, isn't that the direction in which we are going? The inhabitants of Huxley's brave new world are produced in vitro and never really emerge from the bottle. They too have "untrammeled freedom of choice," but it is an illusory freedom, since their controlled encounter with reality presents them only with the experiences and the ambitions that their makers allow. There is no room in their world for virtue, love, or self-sacrifice, since they are accountable for nothing that happens to them and nothing that they do. The lonely "savage," grieving for his mother and nurturing his spirit on Shakespeare, reacts to the spectacle of that world by committing suicide. For it is a world without meaning, a world in which the categories that endow things with moral significance no longer apply.

The Morality of the Body

Huxley's tale reminds us that our moral concepts are developed in vivo, not in vitro. And they are rooted in the very "we" attitude that is threatened by the careless pursuit of mastery. When we envisage situations that involve a reshaping of human nature, so that all those features that traditional morality was designed to regulate—aggression, fragility, the dread of oblivion; love, hope, the thrill of desire—either disappear or are transformed entirely, then we conjure worlds that we cannot understand and that do not in fact contain us. Were we, like Huxley's savage, to find ourselves washed up on these imagined shores, we should be as disoriented and unconsoled as he. The right to life is not a right to immortality but a right to live and die unmolested, a right to pursue the projects that mortals naturally assume, all of which are predicated on their transience. To speak of a "right to life" in a world where life is freed from the conditions that make it meaningful is to lift the concept from the context that provides its sense.

Even if immortality lies forever beyond our reach, the progress of biotechnology has created moral problems of a kind that place their own strain upon the ordinary conscience. Cosmetic surgery, organ transplants, mood-enhancing drugs—all such things have begun to change our conception of the body and its relation to the self. It is often complained against Descartes that he made so radical a distinction between mind and body as to make it impossible to understand how there could be any connection between them. But even Descartes protested that "I am not merely lodged in my body as a pilot in a ship"—implying that there is an intimacy of connec-

tion here that makes it entirely natural to say of my body that it is not mine but *me*. Can we still say that when so much that happens to my body happens by my own design?

On the other hand, the idea that both body and brain are property is gaining ground. Cosmetic surgery (on which Americans spend approximately $10 billion a year) and mood-enhancing drugs make it possible for people to alter their bodies and brains, to appear with new faces and even new personalities, and yet somehow retain that core of self-identity that enables them to say these new bodies and new characters are "theirs." In these and other ways, there arises a separation between self and body of a kind that might lead us once again to entertain ideas of "untrammeled freedom." And the new world of enhanced bodies and shriveled selves will be one dominated by the "I" attitude—a world in which the "we" attitude has retreated into silence. Imagine a race of humans who can not merely live forever but also alter their physiognomy and even their fundamental character at will, who can

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reëngineer their bodies, taking spare parts from others or from embryos, perhaps growing embryos for the purpose. Maybe, since children will be a threat in any case in the world to which these people belong, human embryos will be bred only for spare parts and never allowed that "right to life" that Aubrey de Grey promises to all of us forever. Without doubt these new humans will strive to outdo one another in beauty, strength, cheerfulness, and all the other features that bring success in life—and will, with time, become equally successful, which means, of course, not successful at all.

We can go on imagining futuristic scenarios of this kind, and there is no real limit to them. Techniques now opening before us—cloning, hybridization, genetic manipulation—present possibilities that both fascinate and frighten us. Already researchers have implanted a variety of human genetic sequences into the DNA of mice, so as to induce diseases previously observed only in humans—all in the worthy cause of finding a cure. Such experiments inevitably recall science fiction stories about hybrids of humans and animals. Ordinary people, confronted with these scenarios, will throw up their hands and say, "Don't go there!" This was the reaction of the British Parliament last year when it proposed a law that would forbid the hybridization of human embryos. Interestingly enough, however, scientists already working on the project complained that the government had not understood its value, that important medical breakthroughs were promised, that the research would bring hope to many who are currently suffering from terminal ailments. In other words, the project should be permitted, since the results might be beneficial.

Hubris and Piety

Sherwin Nuland refers to his own "secular spiritual" position, which prompts him to recoil from this kind of radical refashioning of human destiny. I know what he means. Religious people, who see their time on earth as a pilgrimage, will have no difficulty in understanding that some discoveries should not be pursued; didn't death enter the world through the lust for knowledge? There are techniques that we ought not to develop, since in developing them we are playing at God, as Adam played at God in trying to distinguish good and evil for himself. The Greeks described this playing at God as hubris and also as an offense against *sebas*, or piety. And hubris, they believed, brings down the vengeance of Olympus. The Romans took over the idea of piety and made it into the cornerstone of their somewhat godless, or at any rate very earthbound, religion. And the Roman *pietas* corresponds, I believe, to the "secular spiritual" hesitation expressed by Nuland. Piety is a kind of metaphysical humility—a recognition of our dependence and fragility, and of the dangers of meddling too much in nature's secrets. It is another name for the "we" attitude that I have been expounding in this essay, the attitude that asks us to respect the fixed points that we should never displace from their allotted positions in our moral universe.

By putting the problem in that way, however, we endow it with an insoluble character. The "we" attitude, which puts intuitive limits on our desire for knowledge and power, is an attitude that we have every reason to acquire. But it is not a reasonable attitude. On the contrary, it involves a rooted refusal to reason, a determination to draw a line and to take a stand at the point fixed by our moral intuitions. "Don't go there!" is all it has to say to us; and its deliverances are as unpersuasive to the person who does not share them as the taboos of a primitive religion. Indeed, some would

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respond, the Roman concept of piety is no real advance over the Polynesian concept of taboo: these are just two different names for the same fear, the same retreat, the same offense against knowledge and discovery. We have no alternative, as rational creatures, to pursuing the path that knowledge has opened up to us.

Moreover, by closing off particular paths we risk depriving ourselves of the very knowledge that we need if the fixed points are really to be safeguarded. The earth can be saved only if we find alternatives to fossil fuels—and find them soon. Biotechnology may look like a threat to one of our fixed points (human nature), but it may be the final anchor of the other (the earth). For it promises one of the most plausible avenues to sources of clean and renewable energy—for example, fuel generated from biomass by carefully engineered microörganisms *(see "Why Termite Guts Could Bring Better Biofuels" on technologyreview.com)*. And if the fixity of human nature seems to be at risk from biotechnology, we should remember that it is part of our nature to take risks with our nature—to adapt it to our uses in order to enhance our beauty, our knowledge, and our power. Why should it be acceptable to achieve these results through clothes, books, and exercise, and not by transferring a gene or two? If it is a violation of our nature to manipulate our genes, why is it not also a violation of our nature to forbid this? We are free, after all, and attempts to curtail our freedom, when not justified by some urgent need, diminish us.

The Future of Freedom

But what happens to freedom in the posthuman future? Leon Kass's anxiety, that genetic manipulation might permit a new kind of despotism of one generation over the next, is widely shared. If Jack can implant genes into Jill, developing her in vitro according to goals of his own, what remains of Jill's freedom, and how will she react to her creator? Jill will not be a slave, exactly, but many people think that her *designed* nature will put in question her ability to be truly herself in the world. But what, exactly, is the worry?

When Mary Shelley imagined the creation of Frankenstein's lonely monster, she was astute enough to see that if the monster was to be a human replica, it would have to be like us in ways other than its physical appearance and its animal life. It would have to be capable of hope and despair, admiration and contempt, love and hate. And in her story the monster became evil, as you or I might become evil, not because he was made that way, but because he searched the world for love and never found it. As we might put it, programmed into the monster were those moral capacities and emotional needs that are the core of human freedom. It is not that Frankenstein had to implant into the monster some peculiar spark of transcendence so as to endow it with freedom. With speech comes reason, with reason accountability, and with accountability all those emotions and states of mind that are the felt reality of freedom.

A rational freedom means the ability to act upon our conscious decisions, on the basis of reasoned assessments of the options, and thereby to become answerable to others for the things that we do. All rational beings have this ability, since that is what rationality means. We no more remove this freedom from our children by genetic manipulation than we remove it by choosing our sexual partners on the basis of beauty, strength, or intelligence—and thereby increasing the likelihood that those attributes will be passed on to our children. Whatever Jack does to engineer Jill, she will have the freedom to thwart his purposes and to use her powers against him. By being accountable to him, she will force him to be accountable to her. The worst thing Jack could do to Jill is what Frankenstein did to his monster—look on her as in some way outside the sphere of human freedom.

The sphere of freedom is not one of *untrammeled* freedom. It is a sphere of responsibility, in which people pay for their freedoms by accounting for their use. Freedom comes into being through the exercise of rational choice, in the conditions of society, and Jack makes himself answerable for Jill's future in the very fact of freely choosing to influence it. If this is so, then the kind of genetic engineering that frightens Kass might be less of a challenge than he believes. It will not alter what is fixed in human nature, for little in our nature is fixed apart from this attribute that distinguishes us and that makes it impossible for others to control what we do. And Jill, when she emerges from whatever dish she was grown in, will have not only the "I" attitude that comes with freedom but also the "we" attitude that causes her to look around herself and wonder what kind she belongs to, and what environment belongs to her. She might go the way of Frankenstein's monster, offering love and never receiving it. But the chances are that she will be as well adapted to her world as we are to ours, and as repelled by the processes that created her as we might be. And when it is her turn to have children, she will leave their genetic makeup to her gods. TR

Roger Scruton is research professor at the Institute for the Psychological Sciences in Arlington, VA, and the author of more than 30 books, including Modern Philosophy. *He farms in Wiltshire, England, and in Rappahannock County, VA.*

Reviews

Books, artifacts, reports, products, objects

PERSONAL COMPUTING

The "New" Apple

It's only not a computer company in name.

By Simson Garfinkel

In the past five months, Apple has dropped the word "Computer" from its name; settled its long-standing dispute with Beatles music publisher Apple Corps; introduced the Apple TV, a set-top box based on its iTunes technology; and announced that it is getting into the cell-phone business. Apple wants us to believe that it is no longer a computer company but, rather, a digital "lifestyle" company, building a set of high-tech experiences around a core of technologies and designs that are warmer, cleaner, easier to use, and more enjoyable than what its competitors in Seattle and Japan have to offer.

APPLE TV
www.apple.com/appletv

OS X, VERSION 10.5
www.apple.com/macosx/leopard

But peel off the skin and Apple emerges as a computer company that's tried and true. Yes, Apple has the world's largest online music store. Yes, Apple has more than 170 brick-and-mortar stores around the world, which sell a lot more than just laptops. But a deep commitment to computing is what holds this empire together.

Consider this, from Apple's recent quarterly filing with the U.S. Securities and Exchange Commission. Apple is "the only participant in the personal computer industry that controls the design and development of the entire personal computer—from the hardware and operating system to sophisticated applications," the company wrote. "This, along with its products' innovative industrial designs, intuitive ease-of-use, built-in graphics, multimedia and networking capabilities, uniquely positions the Company to offer innovative integrated digital lifestyle solutions." It all starts with computing.

Consider the Apple TV. This misnamed product is really just a little single-board computer with a 40-gigabyte hard drive running software that offers a user interface similar to that of iTunes and Front Row, which have been available on Apple's desktops and laptops for a while. In other words, it's a slightly repackaged Mac Mini—one that's thinner and wider—with a slightly different selection of video outputs. Even the remote control is the same one that Apple sold me with my MacBook and iMac. (To learn a bit about how Apple designs its products, see "Different," p. 54.)

I am not the Apple TV's target audience. This is a box for families that have wide-screen HDTV panels hanging on the walls of their family rooms. In my family we are much happier gathering around my wife's desk and watching movies on the 20-inch iMac that we bought last year. In fact, the Apple TV won't even work with our TV, a 15-year-old, 19-inch RCA; the Apple TV will only output HDMI, DVI, or component video, and our old TV wants composite video. I also noticed that the Apple TV gets quite warm even when it is doing nothing. Presumably, one reason for its thinness is better heat dissipation. (Apple has long had more problems with heat dissipation than other computer companies, because of Steve Jobs's intense dislike of fan noise.)

It's too early to say whether the Apple TV will be a success (if it does fail, it is sure to be quickly forgotten, given how good Apple is at burying mistakes). Nevertheless, in the past few years Apple has enjoyed a return to prominence within the computer industry—and not just because of its designs. In the world of servers and machine rooms, where ease of use and style are largely irrelevant, Apple has emerged as a company that delivers extraordinarily reliable, cost-effective computing hardware. Its rack-mounted Xserve server is showing up in major corporations and in supercomputing clusters. Organizations are even purchasing Apple's Xserve RAID storage array and using it with non-Apple servers running Windows or Unix.

Unlike most of its hardware and software rivals, Apple has eagerly used open standards and open-source software to develop—ironically enough—a system that combines proprietary hardware with proprietary software. Apple's iCal was one of the first widely available desktop calendar programs to adopt the iCalendar standard; Apple embraced iCalendar so early that many

BRIAN STAUFFER

people mistakenly thought Apple had invented it. Instead of creating proprietary e-mail protocols to connect Apple Mail with the company's paid online service, Apple adopted the industry-standard IMAP protocol. The Mac OS ships with the Apache Web server, the Postfix mail server, and the OpenLDAP directory server. All this borrowing is completely legal, and the result is that Apple is able to direct more of its R&D dollars to developing distinguishing technology, since it doesn't have to spend as much on the "plumbing" of today's information infrastructure. That directly benefits customers by lowering Apple's cost of innovation. It also benefits Apple's third-party developers by making Macintosh development not all that different from Linux development, which is generally regarded as a lot easier than developing software for Microsoft Windows.

Leopard

Which brings us to Mac OS X version 10.5, or "Leopard," one of the centerpieces of the "new Apple." According to the company, Leopard will be unveiled "sometime this spring." For now, only developers and perhaps a few lucky reviewers have played with it—and both are bound by the most blood-curdling of nondisclosure agreements not to reveal anything about it. But here's what we can say about the OS, based on the company's public announcements and on those products and services that will be part of it but are already in use.

Leopard is Apple's sixth major OS X release in six years. Maintaining that pace is quite an accomplishment, especially considering that Microsoft didn't release a significant upgrade to its operating system between the launch of Windows XP in 2001 and the release of Vista this year. This contrast reveals more about business strategy than about technical acumen: what Apple has done is move its loyal customers from a software purchase model to a software subscription model. Each of Apple's new releases has offered significant improvements to part—but not all—of the Macintosh system, and each has cost $129.

That's a lot of money for an incremental release, but the lack of license management means that payment is based largely on the honor system. (Compare that with Windows, where activation codes accompany every operating system CD-ROM.) This may lose some sales, but the result is that few Apple customers hate the company the way so many Windows customers hate Microsoft. Apple even sells a "Family Pack" version of its operating system, which lets diehard Mac fans spend an extra $70 for the legal right to install the OS on "up to five" computers in their homes. I bought one last year: it contained exactly the same DVDs that the single-user edition did. The difference is in the buyer's heart.

Mac OS 10.5 will work hand in hand with Apple's fancy online service, .Mac. Priced at $99.95 a year, .Mac gives you an @mac.com e-mail address and a gigabyte of storage accessible through the .Mac Web interface or through Apple's mail application. There is also iDisk, which lets you store files on Apple's servers and share them between computers. On your desktop,

iDisk looks like just another disk drive, but you can also access it through the .Mac website. You can even mount the drive from a Windows computer using a Windows program that Apple provides. The .Mac service also offers one-click Web publishing, which works with any Web-design application but works especially well with Apple's easy-to-use iWeb designer. It's even easy to create password-protected Web pages for family, friends, or business associates.

The power of .Mac—largely ignored by other reviewers—is that it brings to Apple users the same kinds of services that most Windows users get from their corporate IT departments. Think of .Mac as a big Microsoft Exchange Server that automatically synchronizes e-mail, bookmarks, website usernames and passwords, and other kinds of configurations to work with all your Macintosh computers. This is a huge benefit for anyone who has both a Mac laptop and a desktop, but it's also superhandy for people who read their e-mail both on their Macs and remotely, via the Web. And all your .Mac mail and files are cached on your computer, not on a server as with Google's Gmail, so they're available when you don't have Internet connectivity.

With Mac OS 10.5, Apple will dramatically improve the services that .Mac provides to Apple users. For example, iCal will support group scheduling, with calendars that can be viewed by multiple users. And you will be able to synchronize notes, to-do lists, items in the dock, and all application preferences across multiple computers.

On the desktop, Leopard's centerpiece will be Time Machine, a breakthrough application that will back up your Mac to a high-capacity external drive and then allow you to cruise through these backups chronologically. Jun Rekimoto of Sony Computer Science Laboratories in Tokyo pioneered this approach back in the 1990s, calling it "time-machine computing." But whereas Sony largely ignored Rekimoto's work, Apple has taken the idea mainstream.

Being able to browse and restore files from a backup is nothing new—programs like Retrospect and even Microsoft Backup have been doing this for years. The real difference is that Time Machine will be integrated with the Mac's new operating system: you can browse your backups simply by clicking an icon from the Finder. I suspect that Time Machine will frequently be used to recover files that would just be too much bother to restore with other systems. Finally, because Time Machine is an operating service, other programs can use it directly. For example, you can go back in time and see how particular entries in your address book have changed, or find photos that were accidentally deleted from your iPhoto database.

For the initial backup, I believe that Time Machine will take roughly 10 minutes for each gigabyte of data on your system; for the typical desktop or laptop, you should probably budget 20 hours. Afterwards, you can set the system to perform an incremental backup on a regular basis—say, at 4:00 every morning. I imagine that you'll be able to use this in conjunction with the alarm clock that's built into every Mac, so that your computer automatically turns itself on every morning and backs itself up before you awake.

Another area in which Apple has apparently invested time and money is the Mac's parental-controls feature. Since I'm the father of a 10-year-old girl, this is something that immediately caught my eye.

There will be a little additional apple-polishing in the 10.5 release. Apple will further improve the compatibility of its operating system with both Microsoft products and emerging standards. Apple's bare-bones TextEdit will now save text as HTML or in the Microsoft Word 97, 2003 XML, RTF, or Word 2007 formats. Apple's mail program will have a better handle on what to do when mail servers are not available online. And if you type a query into Apple's unified "help" system, it will now search through the menus of the program you're using to find an answer. Since the help function is built directly into the operating system, it will even work with old programs like Microsoft Word.

There are some things I would hope Leopard includes by the time it ships. Users will certainly be able to set up the operating system's firewall to filter incoming data transmissions. But will they be able to put restrictions on outgoing ones, too? If not, the Mac's firewall won't be able to prevent spyware that's running on your computer from reporting on your actions. True, there is currently precious little spyware written for the Mac. But there is some, and it would be good to have some extra protection built into the operating system: as Macs become more popular, the amount of spyware is sure to increase.

I am no Mac bigot: I have a PC running Windows XP on my desk at home, and I use servers running FreeBSD and Linux every day. But the only things I use that PC for are Quicken Home and Business and a scanner that's incompatible with my Mac. When I visit my friends who are still using PCs, all too often I find myself spending half an hour "fixing" their machines so that they don't find them so tremendously frustrating.

I used to tell my friends, "Get a Mac." These days I don't bother. Given iTunes, Apple TV, and the new iPhone, I suspect that my friends will be able to use more and more of Apple's technology from their PCs as time goes on. But they'll still miss out on the totally unified Mac experience—one as firmly rooted in the ideal of the easy-to-use desktop machine as it ever was. TR

Simson Garfinkel researches computer forensics at the Harvard Center for Research on Computation and Society.

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SEARCH

Reintermediation

For the legions of Internet users contributing to new "human-assisted search" sites, no job is too small. **By Wade Roush**

On January 28, a day of calm seas off the California coast, computer scientist Jim Gray left San Francisco on his 40-foot yacht *Tenacious* and made for the Farallon Islands, 43 kilometers beyond the Golden Gate Bridge, where he planned to scatter the ashes of his recently deceased mother. He failed to return that evening.

For the next four days, the U.S. Coast Guard searched the ocean around the Farallons but found no trace of him. Gray's friends and colleagues, however, refused to give up. A technical fellow at Microsoft and a pioneer in the development of database systems and transaction processing, Gray, 63, was one of the most beloved figures in the computer science community. Executives at Amazon, Sun, Oracle, Google, Microsoft, and other companies organized an intense private search, even enlisting a plane owned by NASA—a close cousin of the U-2 spy plane—and a satellite operated by mapping company DigitalGlobe to collect thousands of new images of the areas to which *Tenacious* might have drifted.

Despite all this firepower, though, Gray's friends knew they'd need outside help to analyze the images they accumulated. So engineers at Amazon divided the images into tiles, each showing a 300-by-300-meter square of ocean, and on February 2 they uploaded the tiles to Amazon Mechanical Turk, a website where people can earn micropayments in return for completing quick tasks—such as recognizing objects in photographs—that are difficult for computers but easy for humans. More than 12,000 volunteers spent five days scanning 560,000 images for blobs of white pixels that might be *Tenacious*. They spotted a candidate, but planes dispatched to that area found nothing.

Gray's family called off the search on February 16, and his disappearance remains a mystery. But the massively distributed, Internet-based search for *Tenacious*, probably the largest effort of its kind in history, stands as a tribute to Gray and as a powerful example of the emerging technology of "human-assisted search." Few of the technology's applications are of the life-and-death variety. But having followed it for some time, I believe that it will soon become pervasive, and that it will dramatically change our assumptions and expectations about the search process and about the types of work that can be accomplished using the Internet. In contrast to the Web's famous disintermediating effects in commerce, human-assisted search is a form of "reintermediation"—an acknowledgement that software isn't always king, and that sometimes it helps to have a middleman.

AMAZON MECHANICAL TURK
www.mturk.com

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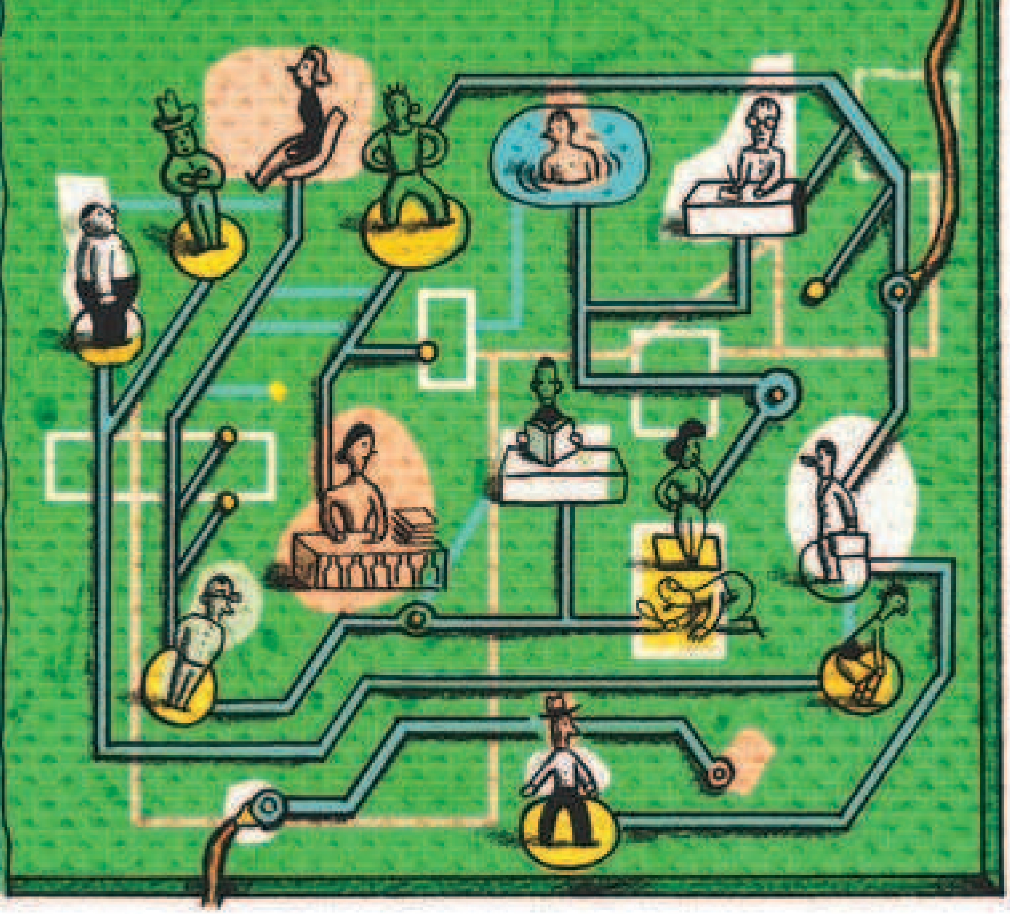
Google's remarkable success at taming the jungle of text-based Web pages fostered the dream among some researchers that all digital information could be indexed, organized, and comprehended algorithmically—that is, using software alone. If this dream ever comes true, it will be far behind schedule. Meanwhile, entrepreneurs at Web companies such as Amazon have begun to show how the brainpower of thousands of Internet users can be harnessed for specific tasks that remain beyond the capabilities of software.

Mechanical Turk, named after an 18th-century automaton that supposedly played chess but actually concealed a human chess master, is at the forefront of this trend. The idea is simple: somebody with a job to be done, such as transcribing a podcast or proofreading a contract, enters the details into a Web page at Amazon (to do this, however, a person needs technical savvy or the help of a Web developer). Mechanical Turk outsources these so-called human intelligence tasks (HITs) to willing workers across the Internet, who earn a small fee for each one they complete.

HITs can be both boring and touchingly human. (A Pasadena family whose Yorkie had been abducted offered workers $0.10 for every time they posted notes about it on forums, message boards, or MySpace pages.) The search for Jim Gray, however, points toward a significant role for the technology in the future. Imagine armies of PC owners reviewing airport security videos from around the country for the face of a single wanted fugitive, or scrutinizing telescope images for signs of dangerous new near-Earth asteroids. The Web provides tools for interaction that are turning people's pattern recognition skills into a valuable commodity.

The "people-powered search" company ChaCha is another case in point. Since last fall, the company has recruited 30,000 live "guides": mostly retirees, college students, and work-at-home moms who labor at their leisure, spending as little or as much time as they like sharing their expertise on the best Web resources in various topic areas. (Guides, who must be invited to join ChaCha by other guides, can earn $5 to $10 per search hour.) The free search service begins with a text box for searching ChaCha's traditional Web index. If a regular search doesn't turn up satisfactory results, a user can click a link labeled "Chat Live with a Guide," which sends the visitor's query to the appropriate human. Once paired with a guide, the visitor receives instant messages containing greetings and, sometimes, requests for clarification. The



MARC ROSENTHAL

guide then selects five or ten promising links on the subject and sends them back to the user's screen, along with the same keyword-related ads that show up beside instant search results and are the company's main revenue source. The results are also added to the ChaCha Web index, which consequently grows in quality over time.

A few dot-com-era companies, such as Webhelp.com, tried to market human-assisted search services and failed. But in the era of MySpace, YouTube, Skype, and instant messaging via phone and PC, people are more ready for the concept of working with a live person online; in fact, they're thirsty for a little human interaction and human wisdom on the Web, at least in the eyes of Brad Bostic, ChaCha's president and chief operating officer. "It's both technology and culture that are changing," Bostic told me. "A few short years ago, e-mail was the standard mechanism for interacting over the Internet. Now people turn to instant messaging and other outlets, not only to gain information but to gain social fulfillment."

I've found ChaCha's guides to be consistently pleasant and straightforward, even if they do sometimes fail to scratch my information itch. To one of my queries, about irrigation for desert gardens, a guide named Navindra responded frankly, "Umm, I am telling you from up front that your info seems a bit hard to find." No worries: Navindra soon transferred me to Fabrice, who was able to locate two makers of drip-irrigation systems. The entire interaction took 22 minutes. I could probably have found the same information faster on my own, using Google, but it certainly wouldn't have left me with the same sociable glow.

I expect that ChaCha searches will go faster and produce better results as the guides gain experience and as the company improves the tools it gives them for plumbing the Web. And Bostic's point—that the average netizen is increasingly comfortable turning to fellow users for information—is part and parcel of the explosion in "social computing," manifested in the great popularity of other user-driven reference sites, such as Wikipedia and Yahoo Answers, and in the proliferation of Internet-based instant messages, which now outnumber voice calls.

Amazon Mechanical Turk, ChaCha, image-tagging startup Polar Rose, collaborative search engine PreFound.com, and other new human-dependent Web ventures are significant because they are the first to exploit a new economic phenomenon: Internet piecework. Humans, it turns out, are even better than computers at completing some big information-intensive tasks such as indexing the Web or searching satellite photos for lost vessels—as long these big jobs are broken into thousands of small ones and distributed to willing workers. That's what the new online tools do, with great efficiency. And companies are already discovering that it doesn't take much to recruit workers—just a chance to earn a few extra bucks, in ChaCha's case, or a humanitarian urge to help in a crisis, in the case of the Jim Gray search.

But whether brokering this type of piecework can become a business big enough to meet the expectations of Wall Street and the venture capital crowd remains to be seen. For now, the companies enabling human-assisted search are putting their faith where dot-com entrepreneurs put theirs—in the Internet's ability to aggregate millions of users, and in Web software and hardware that can process a continuous flood of transactions swiftly and cheaply. "How do you make many small things add up to a big thing? By making your system amenable to handling lots and lots of them," says Peter Cohen, director of the Mechanical Turk project at Amazon. "We wouldn't be doing this unless we thought there was going to be a business here for us."

Computerization and the productivity gains that go with it have plenty of unintended side effects, from longer unemployment lines to the voice-activated phone menus that make it hard to get assistance from a person at your bank or cable company. But the next time you look for help on the Web, it just might come from a human. TR

Wade Roush is a Technology Review *contributing editor.*

Silicon Brains

Computer chips designed to mimic how the human brain works could shed light on our cognitive capacities.
By Emily Singer

PHOTOGRAPHS BY EMILY NATHAN

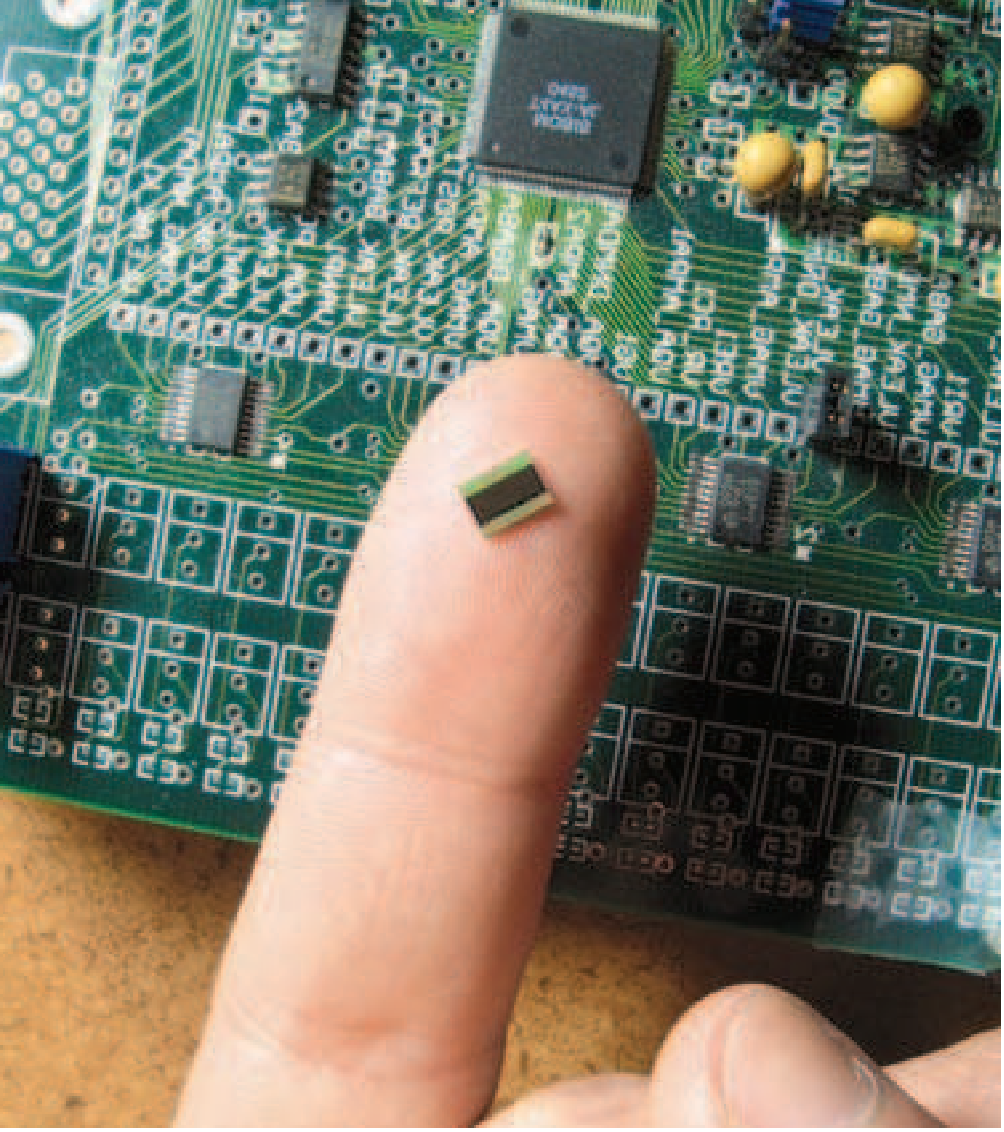
Unlike most neuroscience labs, Kwabena Boahen's lab at Stanford University is spotless—no scattered pipettes or jumbled arrays of chemical bottles. Instead, a lone circuit board, housing a very special chip, sits on a bare lab bench. The transistors in a typical computer chip are arranged for maximal processing speed; but this microprocessor features clusters of tiny transistors designed to mimic the electrical properties of neurons. The transistors are arranged to behave like cells in the retina, the cochlea, or even the hippocampus, a spot deep in the brain that sorts and stores information.

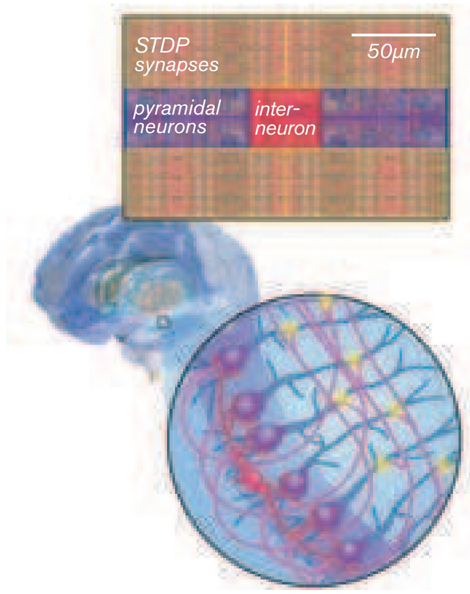
Boahen is part of a small but growing community of scientists and engineers using a process they call "neuromorphing" to build complicated electronic circuits meant to model the behavior of neural circuits. Their work takes advantage of anatomical diagrams of different parts of the brain generated through years of painstaking animal studies by neuroscientists around the world. The hope is that hardwired models of the brain will yield insights difficult to glean through existing experimental techniques. "Brains do things in technically and conceptually novel ways which we should be able to explore," says Rodney Douglas, a professor at the Institute of Neuroinformatics, in Zurich. "They can solve rather effortlessly issues which we cannot yet resolve with the largest and most modern digital machines. One of the ways to explore this is to develop hardware that goes in the same direction."

Among the most intriguing aspects of the brain is its capacity to form memories—something that has fascinated neuroscientists for decades. That capacity appears to be rooted in the hippocampus, damage to which can lead to amnesia.

Extensive studies of neurons in the hippocampus and other parts of the brain have shed some light on how neural behavior gives rise to memories. Neurons encode information in the form of electrical pulses that can be transmitted to other neurons. When two connected neurons repeatedly fire in close succession, the connection between them is strengthened, so that the firing of the first helps trigger the firing of the second. As this process—known to neuroscientists as Hebbian learning—occurs in multiple neighboring cells, it creates webs of connections between different neurons, encoding and linking information.

To better understand how this works, Boahen and graduate student John Arthur developed a chip based on a layer of the hippocampus known as CA3. Sandwiched between two other cellular layers, one that receives input from the cortex and one that sends information back out again, CA3 is thought to be where memory actually happens—where information is stored and linked. Pointing to a diagram of the chip's architecture, Boahen





BRAIN CHIPS **Kwabena Boahen and colleagues use this tiny chip (top left) to study the hippocampus, a brain area important for memory. Transistors in the chip are arranged to mimic specific cells in the hippocampus, which is depicted above. Each cell type in the circular inset corresponds to a color in the chip diagram. Blue pyramidal neurons relay information to each other, across excitatory synapses represented by yellow dots, and to other regions of the hippocampus. Red interneurons manage the behavior of pyramidal cells. A detailed circuit diagram of the chip's architecture—depicting a few neurons and their synapses—is shown on a computer screen (bottom left).**

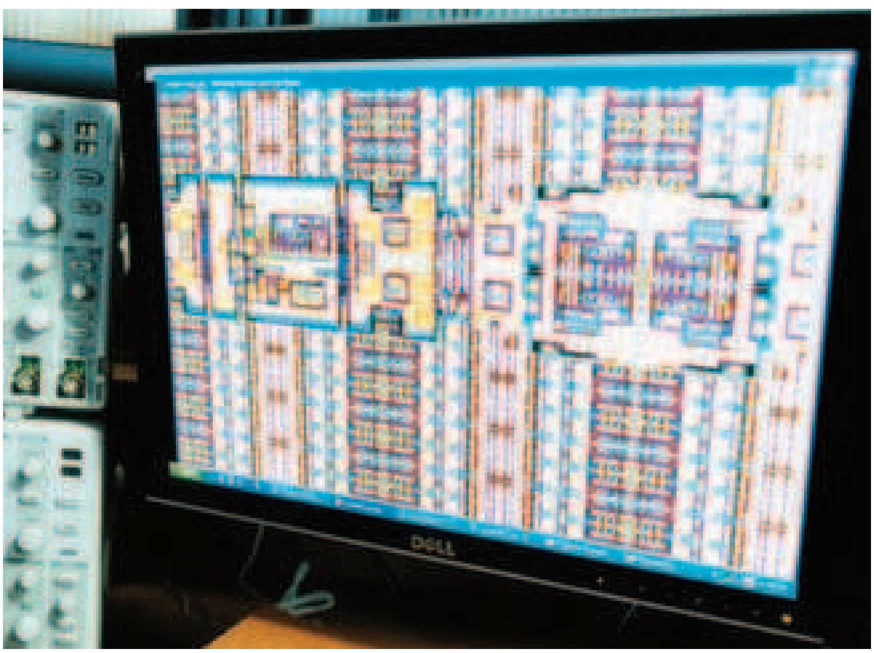
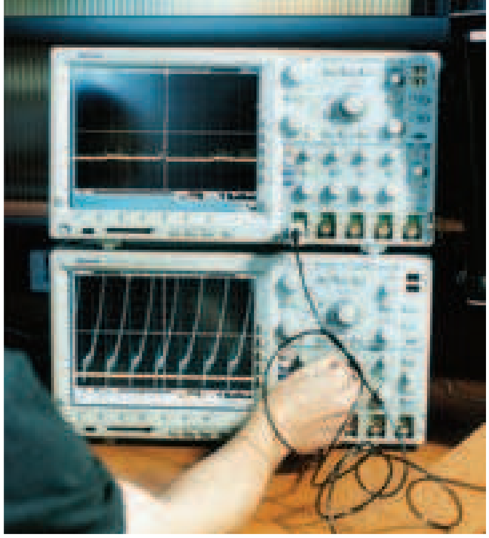


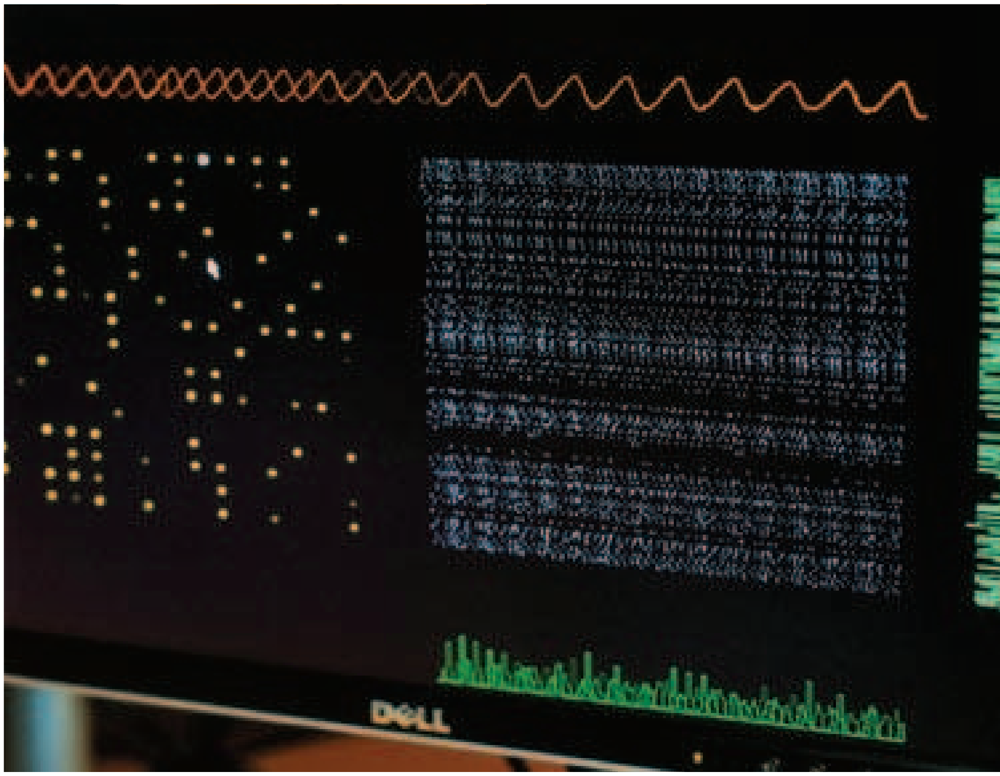
ILLUSTRATION BY LINDA NYE (HIPPOCAMPUS)

explains that each model cell on the chip is made up of a cluster of transistors designed to mimic the electrical activity of a neuron. The silicon cells are arranged in a 32-by-32 array, and each of them is programmed to connect weakly to 21 neighboring cells. To start with, the connections between the cells are turned off, mimicking "silent synapses." (A synapse is a junction between neurons; a silent synapse is one where, if a given neural cell fires, it transmits a slight change in electrical activity to its neighbors, but not enough to trigger the propagation of an electrical signal.)

However, Boahen explains, the chip has the ability to change the strength of these connections, imitating what happens with neurons during Hebbian learning. The silicon cells monitor when their neighbors fire. If a cell fires just before its neighbor does, then the programmed connection between the two cells is strengthened. "We want to capture the associative memory function, so we want connections between the cells to turn on or off depending on



TWO CIRCUIT BOARDS (far left), each with its own neuromorphic chip, are being used to study different aspects of the hippocampus. Scientists use oscilloscopes (near left) to record different properties of the silicon neurons. A computer screen (below) depicts the electrical activity of the cells. The yellow dots, for example, represent the firing rates of individual cells. Bigger dots indicate a higher firing rate.



whether cells are activated together," Boahen says.

Sitting at his desk with the circuit board and a laptop in front of him, Arthur, who is now a postdoc in Boahen's lab, demonstrates the chip's ability to remember. First he sends electrical signals to the chip from the laptop, which also records the output of the chip's silicon neurons. He repeatedly triggers activity only in neurons that form a U shape on the array; his laptop screen shows flashes of light that reproduce that pattern, representing the activity in the chip. Each neuron fires at a slightly different time, constantly monitoring the firing of its 21 connected neighbors. Gradually, connections between the neurons that make up the U are strengthened: the chip has "learned" the pattern. When Arthur then triggers activity in just the upper left corner of the U, flashes of light on the screen spontaneously recreate the rest of the pattern, as electrical activity spreads among silicon neurons on the chip. The chip has effectively recalled the rest of the U.

The Stanford researchers plan to add circuitry to the chip so that it will also model a layer of the hippocampus known as the dentate, which receives signals from the cortex and sends them to CA3. They hope this model will be able to lay down memories that are even more complex. "We want to be able to give it an A and have it recall the whole alphabet," says Boahen.

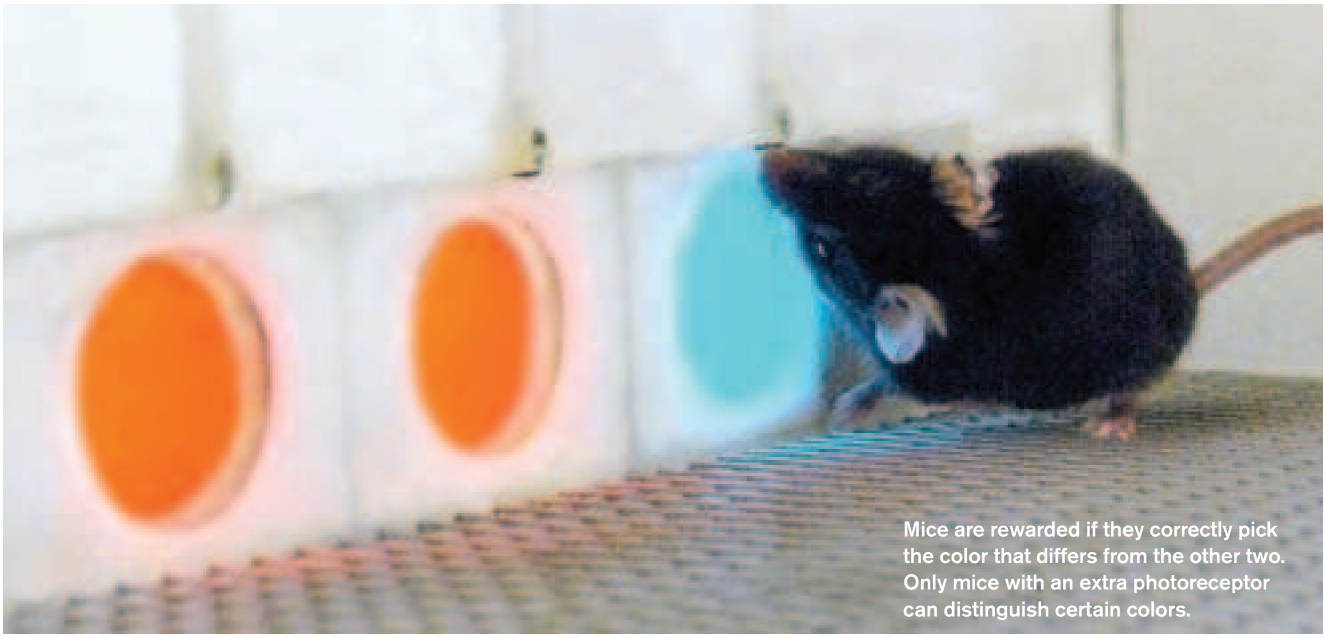
The team is also in the process of developing other neuromorphic chips. Its latest project—and the most ambitious neuromorphic effort anywhere to date—is a model of the cortex, the most recently evolved part of our brain. The intricate structure of the cortex allows us to perform complex computational feats, such as understanding language, recognizing faces, and planning for the future. The model's first-generation design will consist of a circuit board with 16 chips, each containing a 256-by-256 array of silicon neurons.

By creating chips that are able to mimic the cortex, the hippocampus, and the retina, Boahen hopes to better comprehend the brain and, eventually, to design neural prosthetics, such as an artificial retina. "Kwabena is one of the few people straddling two perspectives: those who want to engineer better chips and those who want to understand the brain," says Terry Sejnowski, a computational neuroscientist at the Salk Institute in La Jolla, CA. "I think he's one of those people who is ahead of his time." TR

Emily Singer is the biotechnology and life sciences editor of Technology Review.

From the Labs

Current research in biotechnology, nanotechnology, and information technology



Mice are rewarded if they correctly pick the color that differs from the other two. Only mice with an extra photoreceptor can distinguish certain colors.

GERALD JACOBS

BIOTECHNOLOGY

Mice with Enhanced Color Vision

Mice engineered to have a third photoreceptor can distinguish more colors than normal mice

SOURCE: "Emergence of Novel Color Vision in Mice Engineered to Express a Human Cone Photopigment"
Gerald H. Jacobs et al.
Science 315(5819): 1723–1725

RESULTS: Researchers from Johns Hopkins University and the University of California, Santa Barbara, used genetic engineering to breed mice that have three kinds of photoreceptors, as humans do, instead of two, as mice normally do. After lengthy training, the mice were able to distinguish colors that normal mice could not.

WHY IT MATTERS: Since the result required only genetically induced changes of the photoreceptors and no tweaking of the underlying neural circuitry, the findings suggest that the sensory system is very plastic and can learn to use entirely new information. This could explain how primates, the only animals with trichromatic color vision, developed their color-sensing abilities. Primates may have taken advantage of the extra visual information granted by a new photoreceptor without evolving specialized wiring in the brain.

METHODS: Researchers engineered mice to express the gene for a photosensing protein that can detect red light, which mice usually can't distinguish from green. In behavioral tests, the mice were shown three circles of colored light—two of the same color and one of a different color distinguishable to humans but not to normal mice. After intensive training during which the mice were rewarded for selecting the different color, scientists found that mice with the extra sensor could tell the colors apart while their normal counterparts could not.

NEXT STEPS: Researchers plan to investigate how the visual system in the engineered mice adapted to take advantage of the new information.

Bacteria Made to Harvest Light

A set of genes found in marine microörganisms can give common bacteria the ability to generate energy from light

SOURCE: "Proteorhodopsin Photosystem Gene Expression Enables Photophosphorylation in a Heterologous Host"
Edward F. DeLong et al.
Proceedings of the National Academy of Sciences 104(13): 5590–5595

RESULTS: The common bacterium *E. coli* can be converted into a light-

harvesting organism in a single genetic step. MIT researchers modified the *E. coli* genome to include a string of DNA found in marine microörganisms that can generate energy from light. The resulting bacteria synthesized all the components necessary to duplicate that feat and assembled them in the cell membrane.

WHY IT MATTERS: The genetically modified *E. coli*, which would normally derive their energy from organic compounds like sugars, were able to switch to a diet of sunlight. Similar modifications could lead to bacteria that more efficiently produce biofuels, drugs, and other chemicals, since they could use more of their carbon food sources as material for bioproducts rather than "burning" them for energy.

The findings also shed light on microbial evolution. Scientists had previously found that the genes for the light-harvesting system, which are often found grouped together in the genome, are frequently swapped among different microörganisms in the ocean. The fact that a single genetic transfer can provide cells with all the genes they need to harvest energy from light helps explain how that capacity could travel so widely. (The mechanism for converting light into energy described here, which was discovered just a few years ago, is different from chlorophyll-based photosynthesis.)

METHODS: The genes inserted into the *E. coli* enabled them to synthesize two proteins: proteorhodopsin, which is similar to a protein found in the human retina, and retinal, a light-sensitive molecule that binds to proteorhodopsin. When the proteorhodopsin is bound to retinal and struck with light, it pumps positively charged protons across the cell membrane. That creates an electrical gradient that acts as a source of energy.

NEXT STEPS: The researchers are now working on ways to boost the modified bacteria's ability to harvest and use energy from light.

NANOTECHNOLOGY

Super Lens

New nanostructured materials break the old limits of optical lenses

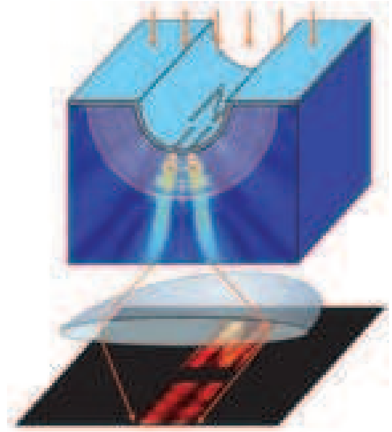
SOURCE: "Far-Field Optical Hyperlens Magnifying Sub-Diffraction-Limited Objects"
Xiang Zhang et al.
Science 315: 1686

RESULTS: Researchers at the University of California, Berkeley, have developed a lens that can resolve details too small for conventional optical microscopes. Using it, they could distinguish two parallel lines 130 nanometers apart; seen through a conventional microscope, the lines looked like a single, thick line.

WHY IT MATTERS: Light-based devices such as optical microscopes have long been limited to resolving or producing features half the wavelength of the light being used. Thus visible light cannot resolve anything smaller than about 200 nanometers. The new lens could make it possible to observe cellular processes never before seen. It could also be used to project images with extremely fine features, increasing the precision of photolithography or enabling much more data to be crammed onto a DVD.

METHODS: The researchers carved a valley shaped like a half-cylinder into a piece of quartz. They then deposited alternating layers of silver and aluminum oxide on the walls of the cylinder. Each layer was just 35 nanometers thick and took the curved shape of the quartz. This arrangement enables the lens to gather more visual information about the object being viewed, which it then passes on to an otherwise conventional microscope.

NEXT STEPS: So far, the lens can be used to view only things in contact with the bottom of its U-shaped valley. It should be possible to build a version of it that does not need to touch the object being viewed.



The new lens (top) gathers information about a nanoscale object and then passes it on to a conventional lens.

XIANG ZHANG

Self-Assembling Batteries

Batteries that make themselves could serve as tiny power sources in micromachines or microelectronics

SOURCE: "Self-Assembling Colloidal-Scale Devices: Selecting and Using Short-Range Surface Forces between Conductive Solids"
Yet-Ming Chiang et al.
Advanced Functional Materials 17(3): 379–389

RESULTS: Thanks to a better understanding of short-range forces between microscopic particles, MIT researchers were able to identify materials that, combined in a solution, will arrange themselves to form a working rechargeable battery. In a prototype, attractive forces cause microscopic carbon particles to aggregate, forming an electrode and attaching to a current collector. Another, preëxisting electrode—a solid slab—repulses the particles, creating the necessary gap between electrodes.

WHY IT MATTERS: Such materials could self-assemble into form-fitting batteries in electronic devices. The materials could also be used in tiny sensors or micromachines.

METHODS: The researchers combined theoretical analysis with precise measurements of the short-range attractive and repulsive forces between

particles of different materials. The measurements were made by attaching particles to the tip of an atomic force microscope. The interplay of forces caused the researchers' chosen materials to sort themselves into a working battery.

NEXT STEPS: To make the battery more rugged, the researchers want to replace the liquid electrolyte used in the prototype with a polymer. Also, future prototypes could use self-assembling particles for both electrodes, not just one.

INFORMATION TECHNOLOGY

Cheaper Lasers

A new type of mirror could make lasers smaller and more efficient

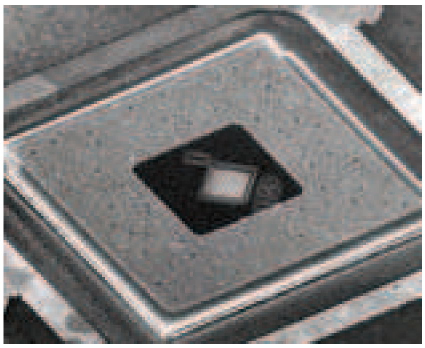
SOURCE: "A Surface-Emitting Laser Incorporating a High-Index-Contrast Subwavelength Grating"
Connie J. Chang-Hasnain et al.
Nature Photonics 1, no. 2 (February 2007): 119–122

RESULTS: Researchers at the University of California, Berkeley, have overhauled one of the main elements of a laser: the mirror. The new mirror is thinner than its predecessors and can be made in fewer steps, simplifying the laser fabrication process and lowering costs. It is also more reflective than previous mirrors, so it could lead to more energy-efficient lasers.

WHY IT MATTERS: Many consumer electronic products use optoelectronic devices such as lasers that could benefit from an efficient, thinner, cheaper mirror. The mirrors currently used in many lasers comprise more than 80 layers of alternating thin films consisting of different materials; each layer adds to the laser's fabrication cost. The new mirror, by contrast, has only one layer.

METHODS: The researchers built their mirror into a common type of laser, called a vertical-cavity surface-emitting laser, that typically consists of two mirrors sandwiching an "active region"—the area in which photons are produced when a current is applied. Photons within the active region reflect off the mirrors, and as they bounce back and forth, their intensity increases. When it gets high enough, they pass through the mirrors, producing a beam of coherent, single-color light.

The new mirror, designed by Connie Chang-Hasnain, professor of electrical engineering and computer science at Berkeley, is a grating composed of thin parallel bars of aluminum gallium arsenide, separated from the rest of the laser by air. The photons from the active region enter



A new type of mirror (square in center) is a fraction of the thickness of conventional mirrors used in semiconductor lasers.

the aluminum gallium arsenide bars; then, because of the optical properties of the junction between the material and the air, they take a 90° turn, reflect off the other bars, come back, and make another 90° turn into the active region. There they bounce back and forth until they are sufficiently amplified, pass through the mirrors, and exit the device.

NEXT STEP: The researchers are working to integrate the mirror into a "tunable" laser, which can emit beams of varying wavelengths of light; such devices would be useful for telecommunications, and for biological and chemical sensors. In addition, they are incorporating the mirror into solar cells, in an effort to improve efficiency. Chang-Hasnain is looking for commercialization partners.

Web Browsing without a Mouse

Eye-tracking user interface could provide an alternative

SOURCE: "EyePoint: Practical Pointing and Selection Using Gaze and Keyboard"
Manu Kumar et al.
CHI 2007, April 28–May 3, 2007, San Jose, CA

RESULTS: Stanford University PhD student Manu Kumar has developed an easy-to-use alternative to the computer mouse: a system that allows a person to point, click, and perform everyday mouse actions by looking at a computer's monitor and tapping a key on its keyboard.

WHY IT MATTERS: User interfaces that use eye-tracking technology have been around for many years and are sometimes used by disabled people. But so far, they haven't been easy enough to use to displace existing technologies.

METHODS: The technology uses standard eye-tracking hardware: embedded in the bezel of a computer monitor are infrared light sources and a camera that captures both the movement of the user's pupil and the reflection of the infrared light off his or her cornea. The user looks at, say, a Web link and then depresses a "hot key" on the keyboard. The area of the screen that's being looked at becomes magnified. Then the user narrows his or her focus within the magnified region and releases the hot key, effectively clicking through to the link.

NEXT STEP: In studies in which participants were asked to type using the keyboard but move the cursor using the eye-tracking system, Kumar recorded an error rate close to 20 percent. He says many errors occur when users think they are focusing on a target that's actually in their peripheral vision, and the eye-tracking technology instead picks up the area they're really looking at. Kumar has developed algorithms to compensate for these errors. TR

CONNIE J. CHANG-HASNAIN

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The Engineer and the Artist

Industrial design has long depended on strange bedfellows.
By Nate Nickerson

In this special design issue, two truths seem to emerge. First, in order to make great things, technology companies must practice collaboration. Bill Moggridge, a cofounder of the design consultancy Ideo, implores us, "Put together a team with a great engineer, a crazy designer, a good businessperson, and a good human-factors scientist or psychologist of some kind, and put them in a room and get them to try to work together" *(see Q&A, p. 30)*. Second, behind companies with well-designed products are leaders who care deeply about design. No company exemplifies that better than Apple, as Daniel Turner reports *(see "Different," p. 54)*.

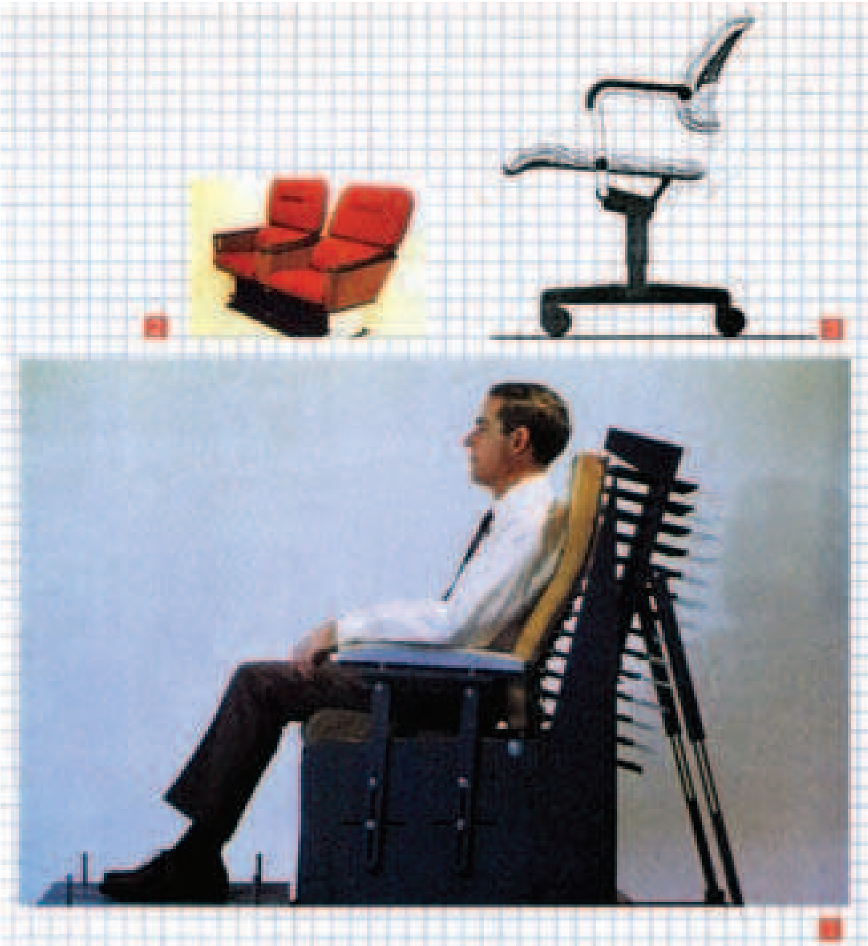
For the February/March 1983 *TR*, Ralph Caplan, a former editor of *Industrial Design*, wrote "Designers and Engineers: Strange but Essential Bedfellows," in which he asserted the importance of those same two truths.

Whatever the project, stereotyping makes strange bedfellows seem stranger than they really are. Designers, like engineers, are insatiably curious about how things work. Engineers, like designers, are attracted to some forms simply because they are nicer than others. I suspect that if design and engineering are to be integrated, it will not be through having designers master high technology or engineers study theories of form, but by exposing members of both disciplines to the humanities.

More generally, the hope for integration lies with individual engineers who are genuinely concerned with the human uses of what they make (including appearance, the use of which is to look at); with industrial designers who know that materials, methods, and structure are as important as a clean line; and with corporate leaders who understand the role of the design process in corporate life. For without the support of top management, no integrated program of design and engineering will succeed. ...

What can managers actually do to improve working relations between designers and engineers? They can give both parties access to essential information and to each other. Designers should be involved very early in a project because their chief contribution may come before the problem is defined. Similarly, engineers need to know marketing objectives because they may impinge upon their work in unpredictable ways, and because they will help make the designers' efforts understandable.

Managers, including design managers, also need to become more sensitive to crediting. Engineers are understandably incensed when they are not given credit for the design aspect of their work, which is, after all, basic.



Industrial designer Niels Diffrient used probes to measure the contours of the human body (1) in order to design airplane seats for American Airlines (2) . The office chair (3) is a sketch by Diffrient of a chair meant to fit the body—and look elegant.

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So who's holding whom over a barrel?